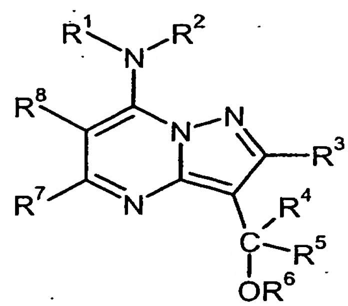
Pyrazolopyrimidines

The invention relates to pyrazolopyrimidines, to a plurality of processes for their preparation and to their use for controlling unwanted microorganisms.

It is already known that certain pyrazolopyrimidines have fungicidal properties (compare DE-A 3 130 633 or FR-A 2 794 745).

However, since the ecological and economical demands made on modern fungicides are increasing constantly, for example with respect to activity spectrum, toxicity, selectivity, application rate, formation of residues and favorable manufacture, and there can furthermore be problems, for example, with resistance, there is a constant need to develop novel fungicides which, at least in some areas, have advantages over those of the prior art.

This invention now provides novel pyrazolopyrimidines of the formula



(I),

in which

R^1 represents optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl or optionally substituted heterocyclyl,

R^2 represents hydrogen or alkyl, or

R^1 and R^2 together with nitrogen atom to which they are attached represent an optionally substituted heterocyclic ring,

R^3 represents hydrogen, halogen, optionally substituted alkyl or optionally substituted cycloalkyl,

R^4 represents hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkenyl, optionally substituted alkynyl or optionally substituted benzyl,

R^5 represents hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkenyl, optionally substituted alkynyl or optionally substituted benzyl,

R^6 represents hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkenyl, optionally substituted alkynyl or optionally substituted benzyl, or

R^5 and $-OR^6$ together represent a radical of the formula $-O-(CH_2)_p-O-$ in which

p represents integers from 1 to 5 and

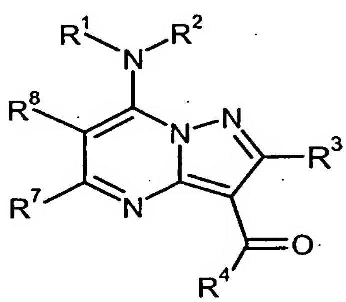
1 to 3 hydrogen atoms may be replaced by methyl, ethyl, hydroxy, methoxy, ethoxy, hydroxymethyl, methoxymethyl or ethoxymethyl,

R^7 represents halogen, CN, optionally substituted alkoxy, optionally substituted alkylthio, optionally substituted akylsulfinyl, optionally substituted alkylsulfonyl or optionally substituted alkyl and

R^8 represents optionally substituted aryl.

Furthermore, it has been found that pyrazolopyrimidines of the formula (I) are obtained when

a) pyrazolopyrimidines of the formula



(II)

in which

R^1, R^2, R^3, R^4, R^7 and R^8 are as defined above

are either

α) reacted with diisobutylaluminum hydride in the presence of aqueous ammonium chloride solution and in the presence of an organic diluent,

or reacted with sodium borohydride in the presence of a diluent,

or

β) reacted with Grignard compounds of the formula

$$R^9 - Mg - X \qquad (III)$$

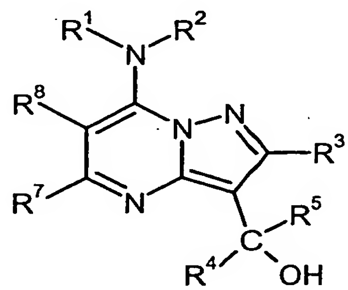
in which

R^9 represents alkyl, alkoxyalkyl, alkenyl, alkynyl or benzyl and

X represents chlorine, bromine or iodine,

in the presence of a catalyst and in the presence of a diluent,

and the pyrazolopyrimidines, obtained according to variant (α) or (β), of the formula



(Ia)

in which

R^1, R^2, R^3, R^4, R^5, R^7 and R^8 are as defined above

are, if appropriate, reacted with compounds of the formula

$$R^{10}\text{-}X^1 \qquad (IV)$$

in which

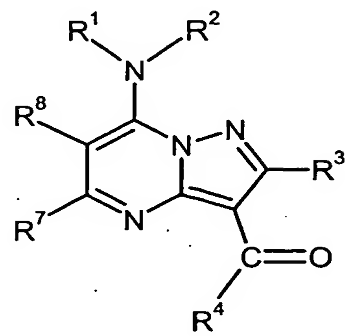
R^{10} represents in each case optionally substituted alkyl, cycloalkyl, alkoxyalkyl, alkenyl, alkynyl or benzyl and

X^1 represents chlorine, bromine, iodine or the radical $R^{10}O\text{-}SO_2\text{-}O\text{-}$,

if appropriate in the presence of a base and if appropriate in the presence of a diluent,

or

b) pyrazolopyrimidines of the formula



(Ia)

in which

R^1, R^2, R^3, R^4, R^7 and R^8 are as defined above,

are reacted with diols of the formula

$$HO-(CH_2)_p-O \qquad (V)$$

in which

p represents integers from 1 to 5 and

1 to 3 hydrogen atoms may be replaced by methyl, ethyl, hydroxy, methoxy, ethoxy, hydroxymethyl, methoxymethyl or ethoxymethyl,

in the presence of a catalyst and, if appropriate, in the presence of a diluent.

Finally, it has been found that the pyrazolopyrimidines of the formula (I) are highly suitable for controlling unwanted microorganisms. Especially, they have strong fungicidal activity and can be used both in crop protection and in the protection of materials.

Depending on the substitution pattern, the compounds according to the invention can, if appropriate, be present as mixtures of different possible isomeric forms, in particular of stereoisomers, such as E and Z, threo and erythro, and also optical isomers, and, if appropriate, also in the form of tautomers. If R^8 is, at both atoms adjacent to the point of attachment, substituted

by different substituents, the compounds in question may be present in a particular stereoisomeric form, i.e. as atropisomers.

The formula (I) provides a general definition of the pyrazolopyrimidines according to the invention. Preference is given to those compounds of the formula (I) in which

R^1 represents alkyl having 1 to 6 carbon atoms which may be mono- to pentasubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxy, alkoxy having 1 to 4 carbon atoms and cycloalkyl having 3 to 6 carbon atoms, or

R^1 represents alkenyl having 2 to 6 carbon atoms which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, hydroxy, alkoxy having 1 to 4 carbon atoms and cycloalkyl having 3 to 6 carbon atoms, or

R^1 represents alkynyl having 3 to 6 carbon atoms which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen, cyano, alkoxy having 1 to 4 carbon atoms and cycloalkyl having 3 to 6 carbon atoms, or

R^1 represents cycloalkyl having 3 to 6 carbon atoms which may be mono- to trisubstituted by identical or different substituents from the group consisting of halogen and alkyl having 1 to 4 carbon atoms, or

R^1 represents saturated or unsaturated heterocyclyl having 5 or 6 ring members and 1 to 3 heteroatoms, such as nitrogen, oxygen and/or sulfur, where the heterocyclyl may be mono- or disubstituted by halogen, alkyl having 1 to 4 carbon atoms, cyano, nitro and/or cycloalkyl having 3 to 6 carbon atoms,

R^2 represents hydrogen or alkyl having 1 to 4 carbon atoms, or

R^1 and R^2 together with the nitrogen atom to which they are attached represent a saturated or unsaturated heterocyclic ring having 3 to 6 ring members, where the heterocycle may contain a further nitrogen, oxygen or sulfur atom as ring member and where the heterocycle may be substituted up to three times by fluorine, chlorine, bromine, alkyl having 1 to 4 carbon atoms and/or haloalkyl having 1 to 4 carbon atoms and 1 to 9 fluorine and/or chlorine atoms,

R^3 represents hydrogen, fluorine, chlorine, bromine, iodine, alkyl having 1 to 4 carbon atoms, haloalkyl having 1 to 4 carbon atoms and 1 to 9 halogen atoms or represents cycloalkyl having 3 to 6 carbon atoms,

R^4 represents hydrogen, alkyl having 1 to 4 carbon atoms, haloalkyl having 1 to 4 carbon atoms in the alkyl moiety, cycloalkyl having 3 to 6 carbon atoms, alkoxyalkyl having 1 or 2 carbon atoms in the alkoxy moiety and 1 to 4 carbon atoms in the alkyl moiety, alkenyl having 2 to 5 carbon atoms, alkynyl having 2 to 5 carbon atoms or benzyl,

R^5 represents hydrogen, alkyl having 1 to 4 carbon atoms, haloalkyl having 1 to 4 carbon atoms in the alkyl moiety, cycloalkyl having 3 to 6 carbon atoms, alkoxyalkyl having 1 or 2 carbon atoms in the alkoxy moiety and 1 to 4 carbon atoms in the alkyl moiety, alkenyl having 2 to 5 carbon atoms, alkynyl having 2 to 5 carbon atoms or benzyl,

R^6 represents hydrogen, alkyl having 1 to 4 carbon atoms, alkoxyalkyl having 1 to 2 carbon atoms in the alkoxy moiety and 1 to 4 carbon atoms in the alkyl moiety, alkenyl having 2 to 5 carbon atoms, alkynyl having 2 to 5 carbon atoms or benzyl, or

R^5 and $-OR^6$ together represent a radical of the formula $-O-(CH_2)_p-O-$

in which

p represents 2, 3 or 4 and

1 or 2 hydrogen atoms may be replaced by methyl, ethyl, hydroxy, methoxy, ethoxy, hydroxymethyl, methoxymethyl or ethoxymethyl,

R^7 represents fluorine, chlorine, bromine, CN, methyl, alkoxy having 1 to 4 carbon atoms, alkylthio having 1 to 4 carbon atoms, alkylsulfinyl having 1 to 4 carbon atoms or alkylsulfonyl having 1 to 4 carbon atoms, and

R^8 represents phenyl which may be mono- to tetratrisubstituted by identical or different substituents from the group consisting of halogen, cyclo, nitro, amino, hydroxy, formyl, carboxy, carbamoyl, thiocarbamoyl;

in each case straight-chain or branched alkyl, alkoxy, alkylthio, alkylsulfinyl or alkylsulfonyl having in each case 1 to 6 carbon atoms;

in each case straight-chain or branched alkenyl or alkenyl having in each case 2 to 6 carbon atoms;

in each case straight-chain or branched haloalkyl, haloalkoxy, haloalkylthio, haloalkylsulfinyl or haloalkylsulfonyl having in each case 1 to 6 carbon atoms and 1 to 13 identical or different halogen atoms;

in each case straight-chain or branched haloalkenyl or haloalkenyloxy having in each case 2 to 6 carbon atoms and 1 to 11 identical or different halogen atoms;

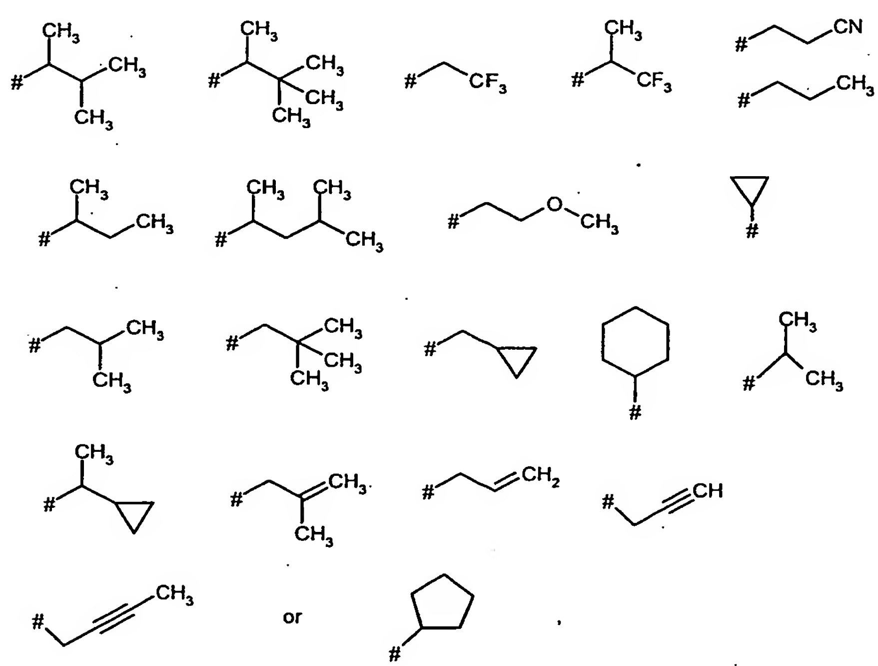
in each case straight-chain or branched alkylamino, dialkylamino, alkylcarbonyl, alkylcarbonyloxy, alkoxycarbonyl, alkylsulfonyloxy, hydroximinoalkyl or alkoximinoalkyl having in each case 1 to 6 carbon atoms in the individual alkyl moieties;

cycloalkyl having 3 to 6 carbon atoms,

2,3-attached 1,3-propanediyl, 1,4-butanediyl, methylenedioxy ($-O-CH_2-O-$) or 1,2-ethylenedioxy ($-O-CH_2-CH_2-O-$), where these radicals may be mono- to polysubstituted by identical or different substituents from the group consisting of halogen, alkyl having 1 to 4 carbon atoms and haloalkyl having 1 to 4 carbon atoms and 1 to 9 identical or different halogenatoms.

Particular preference is given to those pyrazolopyrimidines of the formula (I) in which

R1 represents a radical of the formula



where # denotes the point of attachment,

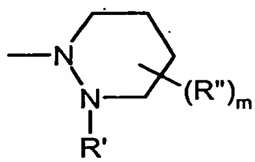
R2 represents hydrogen, methyl, ethyl or propyl, or

R1 and R2 together with the nitrogen atom to which they are attached represent pyrrolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, 3,6-dihydro-1(2H)-piperidinyl or

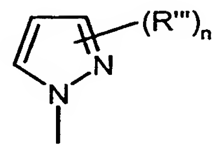
tetrahydro-1(2H)-pyridazinyl, where these radicals may be substituted by 1 to 3 fluorine atoms, 1 to 3 methyl groups and/or trifluoromethyl,

or

R^1 and R^2 together with the nitrogen atom to which they are attached represent a radical of the formula



or



in which

R' represents hydrogen or methyl,

R" represents methyl, ethyl, fluorine, chlorine or trifluoromethyl,

m represents the number 0, 1, 2 or 3, where R" represents identical or different radicals if m represents 2 or 3,

R''' represents methyl, ethyl, fluorine, chlorine or trifluoromethyl

and

n represents the number 0, 1, 2 or 3, where R''' represents identical or different radicals if n represents 2 or 3,

R^3 represents hydrogen, fluorine, chlorine, bromine, iodine, methyl, ethyl, isopropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, trifluoromethyl, 1-trifluoromethyl-2,2,2-trifluoroethyl or heptafluoroisopropyl,

R^4 represents hydrogen, methyl, ethyl, propyl, methoxymethyl, methoxyethyl, alkenyl having 3 or 4 carbon atoms, alkynyl having 3 or 4 carbon atoms or benzyl,

R^5 represents hydrogen, methyl, ethyl, propyl, methoxymethyl, methoxyethyl, alkenyl having 3 or 4 carbon atoms, alkynyl having 3 or 4 carbon atoms or benzyl,

R^6 represents hydrogen, methyl, ethyl, propyl, methoxymethyl, methoxyethyl, alkenyl having 3 or 4 carbon atoms, alkynyl having 3 or 4 carbon atoms or benzyl, or

R^5 and $-OR^6$ together represent a radical of the formula $-O-CH_2-CH_2-O-$ in which 1 or 2 hydrogen atoms may be replaced by methyl, ethyl, hydroxy, methoxy, ethoxy, hydroxymethyl, methoxymethyl or ethoxymethyl,

R^7 represents fluorine, chlorine, bromine, CN, methyl, methoxy, ethoxy, methylthio, methylsulfinyl or methylsulfonyl, and

R^8 represents phenyl which may be mono- to trisubstituted by identical or different substituents from the group consisting of

fluorine, chlorine, bromine, cyano, nitro, formyl, methyl, ethyl, n- or i-propyl, n-, i-, s- or t-butyl, allyl, propargyl, methoxy, ethoxy, n- or i-propoxy, methylthio, ethylthio, n- or i-propylthio, methylsulfinyl, ethylsulfinyl, methylsulfonyl, ethylsulfonyl, allyloxy, propargyloxy, trifluoromethyl, trifluoroethyl, difluoromethoxy, trifluoromethoxy, difluorochloromethoxy, trifluoroethoxy, difluoromethylthio, difluorochloromethylthio, trifluoromethylthio, trifluoromethylsulfinyl, trifluoromethylsulfonyl, trichloroethynyloxy, trifluoroethynyloxy, chloroallyloxy, iodopropargyloxy, methylamino, ethylamino, n- or i-propylamino, dimethylamino, diethylamino, acetyl, propionyl, acetyloxy, methoxycarbonyl, ethoxycarbonyl, hydroximinomethyl, hydroximinoethyl, methoximinomethyl, ethoximinomethyl, methoximinoethyl, ethoximinoethyl, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl,

2,3-attached 1,3-propanediyl, methylenedioxy ($-O-CH_2-O-$) or 1,2-ethylenedioxy ($O-CH_2-CH_2-O$), where these radicals may be mono- or polysubstituted by identical or different substituents from the group consisting of fluorine, chlorine, methyl, ethyl, n-propyl, i-propyl and trifluoromethyl.

A very particularly preferred group of compounds according to the invention are pyrazolopyrimidines of the formula (I) in which

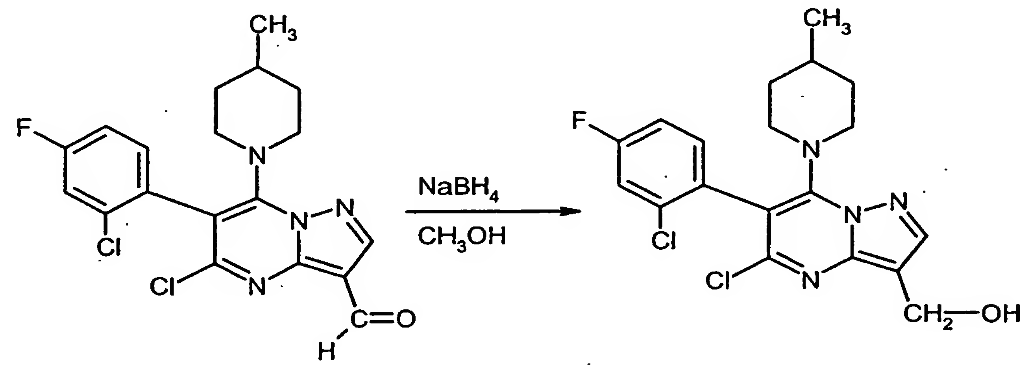
R^1, R^2, R^3, R^4, R^5 and R^6 have the particularly preferred meanings given above,

R^7 represents fluorine, chlorine, bromine, CN, methyl, methoxy or methythio and

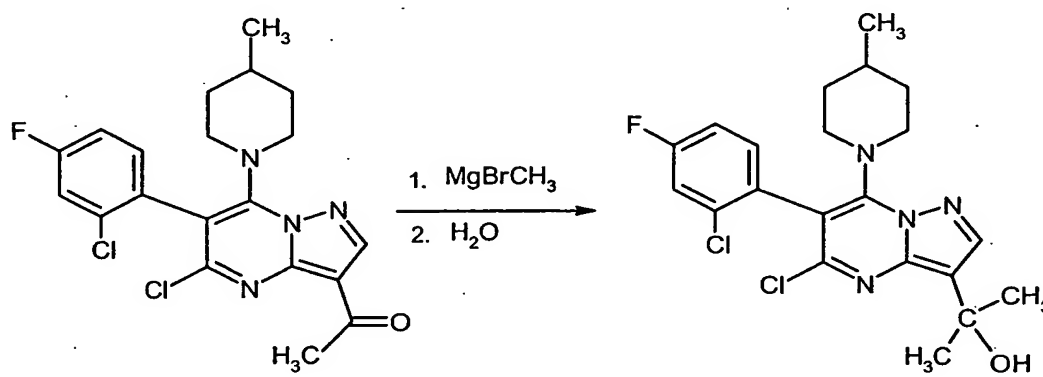
R^8 represents 2,4-, 2,5- or 2,6-disubstituted phenyl or 2-substituted phenyl or represents 2,4,6-trisubstituted phenyl, suitable substituents being the radicals mentioned in the context of the enumeration of the particularly preferred definitions.

The radical definitions mentioned above can be combined with one another as desired. Moreover, individual definitions may not apply.

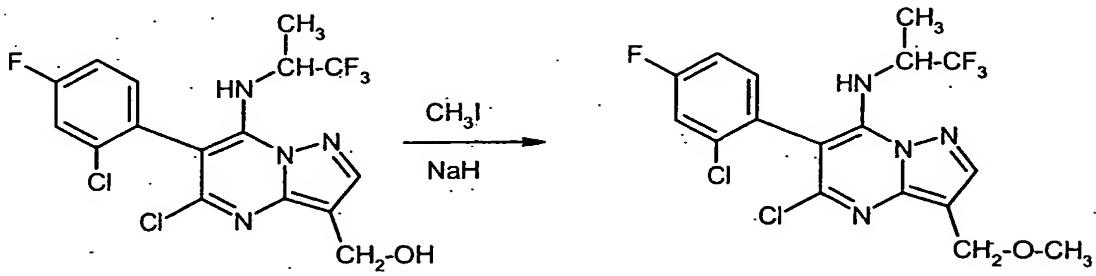
Using 3-formyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methylpiperidino)pyrazolo[1,5-a]-pyrimidine as starting material and sodium borohydride as reaction component, the course of the process (a, variant α) according to the invention can be illustrated by the formula scheme below.



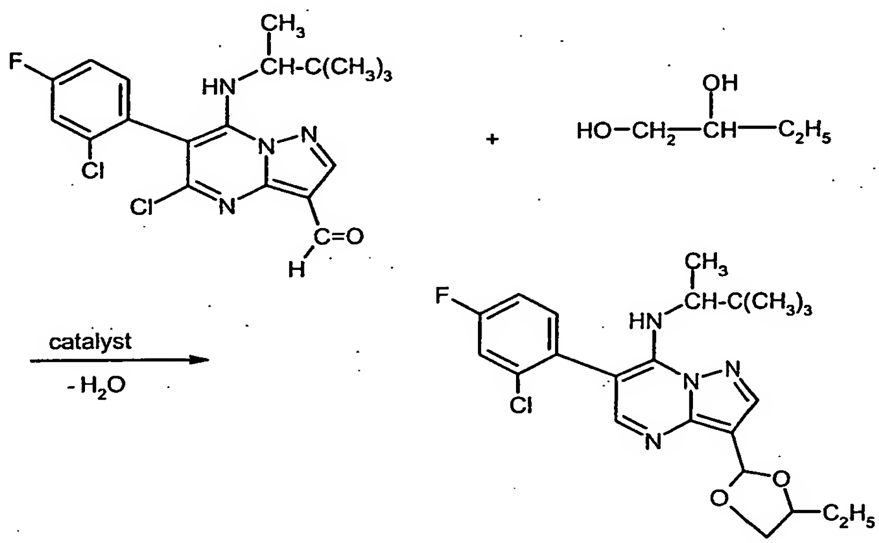
Using 3-methylcarbonyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methylpiperidino)pyrazolo[1,5-a]pyrimidine as starting material and methyl magnesium bromide as reaction component, the course of the process (a, variant β) according to the invention can be illustrated by the formula scheme below



Using 3-hydroxymethyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(2,2,2-trifluoroisopropylamino)-pyrazolo[1,5-a]pyrimidine as starting material and methyl iodide as reaction component, the course of the second stage of the process (a) according to the invention can be illustrated by the formula scheme below.



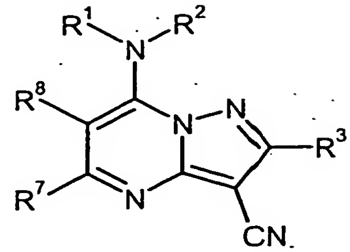
Using 3-formyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(3,3-dimethylbut-2-ylamino)pyrazolo[1,5-a]pyrimidine as starting material and butane-1,2-diol as a reaction component, the course of the process (b) according to the invention can be illustrated by the formula scheme below.



The formula (II) provides a general definition of the pyrazolopyrimidines required as starting materials for carrying out the process (a) according to the invention. In this formula, R^1, R^2, R^3, R^4, R^7 and R^8 preferably have those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for these radicals.

The pyrazolopyrimidines of the formula (II) are obtained when

c) pyrazolopyrimidine derivatives of the formula



(VI)

in which

R^1, R^2, R^3, R^7 and R^8 are as defined above,

are either

α) reacted with diisobutylaluminum hydride in the presence of aqueous ammonium solution and in the presence of an organic diluent,

or

β) reacted with Grignard compounds of the formula

$$R^9\text{-Mg-X} \qquad \text{(III)}$$

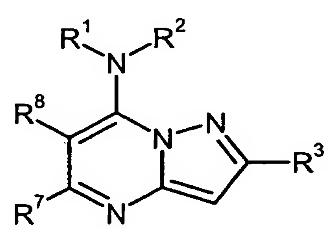
in which

R^9 and X are as defined above,

in the presence of a diluent and, if appropriate, in the presence of a catalyst,

or

d) pyrazolopyrimidines of the formula

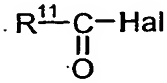


(VII)

in which

R^1, R^2, R^3, R^7 and R^8 are as defined above,

are reacted with acid halides of the formula



(VIII)

in which

R^{11} represents alkyl, alkoxyalkyl, alkenyl, alkynyl or benzyl and

Hal represents chlorine or bromine,

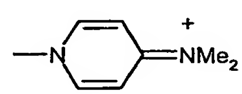
or

with acid anhydrides or other activated carboxylic acid derivatives of the formula

$$R^{12} - COX^{1} \qquad \text{(IX)}$$

in which

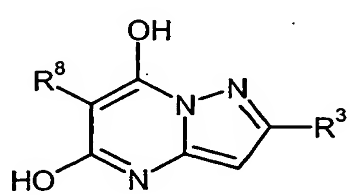
R^{12} represents alkyl, alkoxyalkyl, alkenyl, alkynyl or benzyl and

X^{1} represents O-CO-R^{12} or a radical of the formula ,

in each case in the presence of a catalyst and in the presence of a diluent,

or

e) hydroxypyrazolopyrimidines of the formula

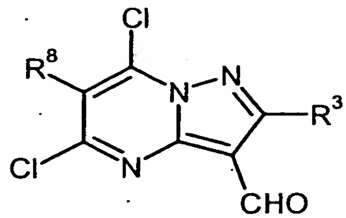


(X)

in which

R^3 and R^8 are as defined above,

are reacted with phosphorus oxychloride in the presence of dimethylformamide and, if appropriate, subsequently reacted with phosphorus pentachloride, and the resulting halopyrazolopyrimidines of the formula

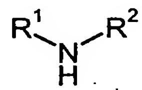


(XI)

in which

R^3 and R^8 are as defined above,

are reacted with amines of the formula



(XII)

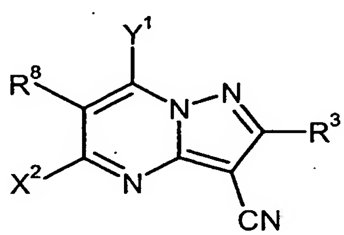
in which

R^1 and R^2 are as defined above,

if appropriate in the presence of a catalyst, if appropriate in the presence of an acid binder and if appropriate in the presence of a diluent.

The pyrazolopyrimidine derivatives of the formula (VI) required as starting materials for carrying out the process (c) are obtained when

f) halopyrazolopyrimidines of the formula



(XIII)

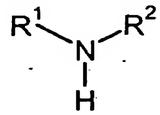
in which

R^3 and R^8 are as defined above,

X^2 represents halogen and

Y^1 represents halogen,

are reacted with amines of the formula



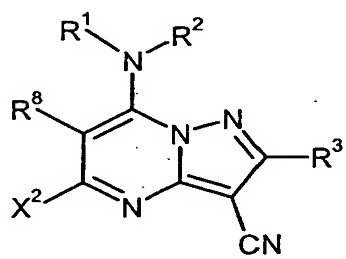
(XII)

in which

R^1 and R^2 are as defined above,

if appropriate in the presence of a diluent, if appropriate in the presence of a catalyst and if appropriate in the presence of an acid acceptor,

and the resulting cyano compounds of the formula



(VIa)

in which

R^1, R^2, R^3, R^8 and X^2 are as defined above,

are, if appropriate, in a second step, reacted with compounds of the formula

R^{13}-Me (XIV)

in which

R^{13} represents optionally substituted alkoxy, optionally substituted alkylthio, optionally substituted alkylsulfinyl or optionally substituted alkylsulfonyl and

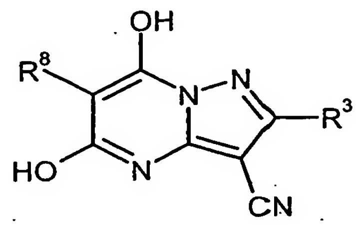
Me represents sodium or potassium,

if appropriate in the presence of a diluent.

The halopyrazolopyrimidines of the formula (XIII) are known or can be prepared by known methods (cf. DE-A 103 28 996 and PCT/EP 03/05159).

Thus, halopyrazolopyrimidines of the formula (XIII) are obtained when

g) dihydroxypyrazolopyrimidines of the formula



(XVI)

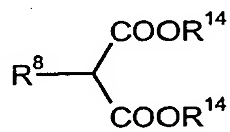
in which

R^3 and R^8 are as defined above,

are reacted with halogenating agents, if appropriate in the presence of a diluent.

The dihydroxypyrazolopyrimidines of the formula (XV) obtained when

(h) arylmalonic esters of the formula



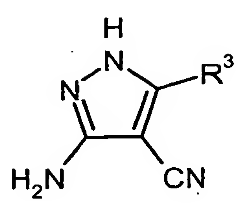
(XVI)

in which

R^8 is as defined above and

R^{14} represents alkyl,

are reacted with aminopyrazoles of the formula



(XVII)

in which

R^3 is as defined above,

if appropriate in the presence of a diluent and if appropriate in the presence of a base.

The formula (XVI) provides a general definition of the arylmalonic esters required as starting materials for carrying out the process (h). In this formula, R^8 preferably has those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for this radical. R^{14} preferably represents alkyl having 1 to 4 carbon atoms, particularly preferably methyl or ethyl.

The arylmalonic esters of the formula (XVI) are known or can be prepared by known methods (cf. US-A 6 156 925).

The aminopyrazoles of the formula (XVII) are likewise known or can be prepared by known methods.

Suitable diluents for carrying out the process (h) are all customary inert organic solvents. Preference is given to using aliphatic, alicyclic or aromatic hydrocarbons, such as petroleum ether, hexane, heptane, cyclohexane, methylcyclohexane, benzene, toluene, xylene or decalin; halogenated hydrocarbons, such as chlorobenzene, dichlorobenzene, dichloromethane, chloroform, carbon tetrachloride, dichloroethane or trichloroethane; ethers, such as diethyl ether, diisopropyl ether, methyl t-butyl ether, methyl t-amyl ether, dioxane, tetrahydrofuran, 1,2-dimethoxyethane, 1,2-diethoxyethane or anisole; nitriles, such as acetonitrile, propionitrile, n- or i-butyronitrile or benzonitrile; amides, such as N,N-dimethylformamide, N,N-dimethylacetamide, N-methyl-formanilide, N-methylpyrrolidone or hexamethylphosphoric triamide; esters, such as methyl acetate or ethyl acetate; sulfoxides, such as dimethyl sulfoxide; sulfones, such as sulfolane; alcohols, such as methanol, ethanol, n- or i-propanol, n-, i-, sec- or tert-butanol, ethanediol, propane-1,2-diol, ethoxyethanol, methoxyethanol, diethyleneglycol monomethyl ether, diethylene glycol monoethyl ether; amines, such as tri-n-butylamine, or carboxylic acids, such as acetic acid.

Suitable strong bases for the carrying out the process (h) are, preferably, alkaline earth metal or alkali metal hydrides or alkoxides and also alkali metal amides. Sodium hydride, sodium amide, sodium methoxide, sodium ethoxide and potassium tert-butoxide may be mentioned by way of example.

When carrying out the process (h), and also when carrying out the other processes of the present patent application, the operations are generally carried out under atmospheric pressure. However, it is also possible to work under elevated pressure or, as long as no highly volatile reaction components are present, under reduced pressure.

When carrying out the process (h), the reaction temperatures can in each case be varied within a relatively wide range. In the absence of bases, the process is generally carried out at temperatures

between 100°C and 250°C, preferably between 120°C and 200°C. In the presence of bases, the process is generally carried out at temperatures between 20°C and 120°C, preferably between 20°C and 80°C.

When carrying out the process (h), in general from 1 to 15 mol, preferably from 1 to 8 mol, of aminopyrazole of the formula (XVII) are employed per mole of arylmalonic ester of the formula (XVI). Work-up is carried out by customary methods.

Suitable halogenating agents for carrying out the process (g) are all customary reagents suitable for exchanging hydroxy groups attached to carbon for halogen. Preference is given to using phosphorus trichloride, phosphorus tribromide, phosphorus pentachloride, phosphorus oxychloride, phosgene, thionyl chloride, thionyl bromide or mixtures thereof. The corresponding fluorine compounds of the formula (XIII) can be prepared from the chlorine or bromine compounds by way of reaction with potassium fluoride.

Suitable diluents for carrying out the process (g) are all organic solvents customary for such halogenations. Preference is given to using aliphatic, alicyclic or aromatic hydrocarbons, such as petroleum ether, hexane, heptane, cyclohexane, methylcyclohexane, benzene, toluene, xylene or decalin; halogenated hydrocarbons, such as chlorobenzene, dichlorobenzene, dichloromethane, chloroform, carbon tetrachloride, dichloroethane or trichloroethane.

However, it is also possible for the halogenating agent for its part or for a mixture of halogenating agent and one of the diluents mentioned to serve as diluent.

When carrying out the process (g), the reaction temperatures can be varied within a relatively wide range. In general, the process is carried out at temperatures between 20°C and 150°C, preferably between 40°C and 120°C.

When carrying out the process (g), in each case an excess of halogenating agent is employed per mole of dihydroxypyrazolopyrimidine of the formula (XV). Work-up is carried out by customary methods.

The formula (XIII) provides a general definition of the halopyrazolopyrimidines as starting materials for carrying out the process (f). In this formula, R^3 and R^8 preferably have those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for these radicals. X^2 and Y^1 each preferably represent fluorine, chlorine or bromine, particularly preferably fluorine or chlorine.

The formula (XII) provides a general definition of the amines required as reaction components for carrying out the process (f). In this formula, R^1 and R^2 preferably have those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for these radicals.

The formula (XIV) provides a general definition of the compounds required as reaction components in the second step of the process (f). In this formula, R^{13} preferably represents alkoxy having 1 to 4 carbon atoms, alkylthio having 1 to 4 carbon atoms, alkylsulfinyl having 1 to 4 carbon atoms or alkylsulfonyl having 1 to 4 carbon atoms. Me also preferably represents sodium or potassium.

Particular preference is given to compounds of the formula (XIV) in which R^{13} represents methoxy, ethoxy, methylthio, methylsulfinyl or methylsulfonyl and Me represents sodium or potassium.

The amines of the formula (XII) and also the compounds of the formula (XIV) are known or can be prepared by known methods.

Suitable diluents for carrying out the first step of the process (f) are all customary inert organic solvents. Preference is given to using halogenated hydrocarbons, such as, for example, chlorobenzene, dichlorobenzene, dichloromethane, chloroform, carbon tetrachloride, dichloroethane or trichloroethane; ethers, such as diethyl ether, diisopropyl ether, methyl t-butyl ether, methyl t-amyl ether, dioxane, tetrahydrofuran, 1,2-dimethoxyethane, 1,2-diethoxyethane or anisole; nitriles, such as acetonitrile, propionitrile, n- or i-butyronitrile or benzonitrile; amides, such as N,N-dimethylformamide, N,N-dimethylacetamide, N-methylformanilide, N-methylpyrrolidone or hexamethylphosphoric triamide; esters, such as methyl acetate or ethyl acetate; sulfoxides, such as dimethyl sulfoxide; sulfones, such as sulfolane.

Suitable acid acceptors for carrying out the first step of the process (f) are all inorganic or organic bases customary for such reactions. Preference is given to using alkaline earth metal or alkali metal hydrides, hydroxides, amides, alkoxides, acetates, carbonates or bicarbonates, such as, for example, sodium hydride, sodium amide, lithium diisopropylamide, sodium methoxide, sodium ethoxide, calcium tert-butyloxide, sodium hydroxide, potassium hydroxide, sodium acetate, potassium acetate, calcium acetate, sodium carbonate, potassium carbonate, potassium bicarbonate and sodium bicarbonate, and furthermore, ammonium compounds, such as ammonium hydroxide, ammonium acetate and ammonium carbonate, and also tertiary amines, such as trimethylamine, triethylamine, tributylamine, N,N-dimethylaniline, N,N-dimethylbenzylamine, pyridine, N-methylpi-

peridine, N-methylmorpholine, N,N-dimethylaminopyridine, diazabicyclooctane (DABCO), diazabicyclononene (DBN) or diazabicycloundecene (DBU).

Suitable catalysts for carrying out the first step of the process (f) are all reaction promoters customary for such reactions. Preference is given to using fluorides, such as sodium fluoride, potassium fluoride, or ammonium fluoride.

When carrying out the first step of the process (f), the reaction temperatures can be varied within a relatively wide range. In general, the process is carried out at temperatures between 0°C and 150°C, preferably at temperatures between 0°C and 80°C.

When carrying out the first step of the process (f), in general from 0.5 to 10 mol, preferably from 0.8 to 2 mol, of amine of the formula (XIII) are employed per mole of halopyrazolopyrimidine of the formula (XIII). Work-up is carried out by customary methods.

Suitable diluents for carrying out the second step of the process (f) are all customary inert inorganic solvents. Preference is given to using halogenated hydrocarbons, such as, for example, chlorobenzene, dichlorobenzene, dichloromethane, chloroform, carbon tetrachloride, dichloroethane or trichloroethane; ethers, such as diethyl ether, diisopropyl ether, methyl t-butyl ether, methyl t-amyl ether, dioxane, tetrahydrofuran, 1,2-dimethoxyethane, 1,2-diethoxyethane or anisole; nitriles, such as acetonitrile, propionitrile, n- or i-butyronitrile or benzonitrile; amides, such as N,N-dimethylformamide, N,N-dimethylacetamide, N-methylformanilide, N-methylpyrrolidone or hexamethylphosphoric triamide; esters, such as methyl acetate or ethyl acetate; sulfoxides, such as dimethylsulfoxide; sulfones, such as sulfolane.

When carrying out the second step of the process (f), the reaction temperatures can also be varied within a relatively wide range. In general, the process is carried out at temperatures between 0°C and 150°C, preferably between 20°C and 100°C.

When carrying out the second step of the process (f), the cyano compound of the formula (VIa) in question is reacted with an equivalent amount or with an excess of a compound of the formula (XIV). Work-up is carried out by customary methods.

The formula (III) provides a general definition of the Grignard compounds required as reaction components for carrying out the process (a, variant β) and the process (c, variant β) according to the invention. In this formula, R^9 preferably represents alkyl having 1 to 4 carbon atoms, alkoxyalkyl having 1 or 2 carbon atoms in the alkoxy moiety and 1 to 4 carbon atoms in the alkyl moiety, alkenyl having 2 to 5 carbon atoms, alkynyl having 2 to 5 carbon atoms or benzyl. X also preferably represents chlorine, bromine or iodine.

Particular preference is given to those compounds of the formula (III) in which

R^9 represents methyl, ethyl, propyl, methoxymethyl, methoxyethyl, alkenyl having 3 or 4 carbon atoms, alkynyl having 3 or 4 carbon atoms or benzyl and

X represents chlorine, bromine or iodine.

The Grignard compounds of the formula (III) are known or can be prepared by known methods.

Suitable diluents for carrying out the process (c, variant α) are all customary inert organic solvents. Preference is given to using aliphatic or aromatic, optionally halogenated hydrocarbons, such as toluene, dichloromethane, chloroform or carbon tetrachloride.

When carrying out the process (c, variant α), the reaction temperatures can be varied within a relatively wide range. In general, the process is carried out at temperatures between -80°C and +20°C, preferably between -60°C and +10°C.

When carrying out the process (c, variant α), in general an equivalent amount or else an excess, preferably from 1.1 to 1.2 mol, of diisobutylaluminum hydride is employed per mole of pyrazolopyrimidine of the formula (VI), and an excess of aqueous ammonium chloride solution is then added. Work-up is carried out by customary methods. In general, the reaction mixture is acidified, the organic phase is separated off, the aqueous phase is extracted with a poorly water-miscible organic solvent and the combined organic phases are washed, dried and concentrated under reduced pressure.

Suitable catalysts for carrying out the process (c, variant β) are all reaction promoters customary for Grignard reactions. Potassium iodide and iodine may be mentioned by way of example.

Suitable diluents for carrying out the process (c, variant β) are all inert organic solvents customary for such reactions. Preference is given to using ethers, such as diethyl ether, dioxane or tetrahydrofuran, furthermore aromatic hydrocarbons, such as toluene, and also mixtures of ethers and aromatic hydrocarbons, such as toluene/tetrahydrofuran.

When carrying out the process (c, variant β), the reaction temperatures can be varied within a certain range. In general, the process is carried out at temperatures between -20°C and +100°C, preferably between 0°C and 80°C.

When carrying out the process (c, variant β), in general from 2 to 3 mol of Grignard compound of the formula (III) are employed per mole of pyrazolopyrimidine derivative of the formula (VI). This is followed by an aqueous work-up according to customary methods.

Pyrazolopyrimidines of the formula (II) can also be prepared by processes (d) and (e).

The formula (VII) provides a general definition of the pyrazolopyrimidines required as starting materials for carrying out the process (d). In this formula, R^1, R^2, R^3, R^7 and R^8 preferably have those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for these radicals.

The pyrazolopyrimidines of the formula (VII) are known or can be prepared by known methods.

The formulae (VIII) and (IX) provide a general definition of the activated carboxylic acid derivatives, such as acid halides and acid anhydrides, required as reaction components for carrying out the process (d). In the formula (VIII), R^{11} preferably represents alkyl having 1 to 4 carbon atoms, alkoxyalkyl having 1 or 2 carbon atoms in the alkyl moiety and 1 to 4 carbon atoms in the alkyl moiety, alkenyl having 2 to 5 carbon atoms, alkynyl having 2 to 5 carbon atoms or benzyl. Hal also preferably represents chlorine or bromine.

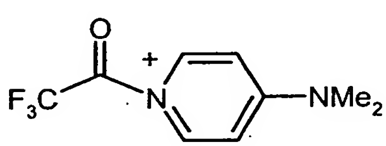
Particular preference is given to acid halides of the formula (VIII) in which

R^{11} represents methyl, ethyl, propyl, methoxymethyl, methoxyethyl, alkenyl having 3 or 4 carbon atoms, alkynyl having 3 or 4 carbon atoms or benzyl

and

Hal represents chlorine or bromine.

A preferred activated carboxylic acid derivative of the formula (IX) is, for example, the commercially available



(Synthesis 1996 (9), 1093).

In the formula (IX), R^{12} preferably represents alkyl having 1 to 4 carbon atoms, particularly preferably methyl, ethyl or propyl.

Both the acid halides of the formula (VIII) and the acid anhydrides of the formula (IX) are known or can be prepared by known methods.

Suitable catalysts for carrying out the process (d) are all reaction promoters customarily used for Friedel-Crafts reactions. Preference is given to using Lewis acids, such as aluminum trichloride, aluminum tribromide and iron(III) chloride.

Suitable diluents for carrying out the process (d) are all inert organic solvents customary for such Friedel-Crafts reactions. Preference is given to using ethers, such as diethylether, methyl tert-butyl ether, dioxane and tetrahydrofuran, and also carbon disulfide.

When carrying out the process (d), the reaction temperatures can be varied within a certain range. In general, the process is carried out at temperatures between -10°C and +100°C, preferably between 0°C and 60°C.

When carrying out the process (d), in general from 1 to 5 mol, preferably from 1 to 2 mol, of acid halide of the formula (VIII) and from 1.1 to 5 mol, preferably from 1.1 to 3 mol, of catalyst, or from 1 to 5 mol, preferably from 1 to 2 mol, of acid anhydride of the formula (IX) and from 2.1 to 6 mol, preferably from 2.1 to 4 mol, of catalyst are employed per mole of pyrazolopyrimidine of the formula (VII). In general, the reaction components are initially added at low temperature and, after the initially vigorous reaction has ceased, the mixture is slowly heated to reflux temperature. Work-up is carried out by customary methods.

The formula (X) provides a general definition of the hydroxypyrazolopyrimidines required as starting materials for carrying out the process (e). In this formula, R^3 and R^8 preferably have those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for these radicals.

The hydroxypyrazolopyrimidines of the formula (X) can be prepared by process (h) if aminopyrazoles of the formula (XVII) are used which, instead of the CN group, carry a hydrogen atom.

The first step of the process (e) is carried out under the conditions of Vilsmeier formulation using phosphorus oxychloride in the presence of dimethylformamide. Here, it is also possible to add phosphorus pentachloride as chlorinating agent.

When carrying out the first step of the process (e), the reaction temperatures can be varied within a relatively wide range. In general, the process is carried out at temperatures between -10°C and +150°C, preferably between 0°C and 120°C.

When carrying out the first step of the process (e), in general from 2 to 5 mol of dimethylformamide, from 5 to 15 mol of phosphorus oxychloride and, if appropriate, from 0 to

2 mol of phosphorus pentachloride are employed per mole of hydroxypyrazolopyrimidine of the formula (X). Work-up is carried out by customary methods.

Suitable for carrying out the second step of the process (e) are the amines of the formula (XII) and those catalysts, acid binders and diluents which have already been mentioned in connection with the description of the process (f). The reaction temperatures and the other reaction conditions also correspond to those which are used in the case of the process (f).

The formula (IV) provides a general definition of the compounds furthermore required as reaction components for carrying out the process (a) according to the invention. In this formula, R^{10} preferably represents alkyl having 1 to 4 carbon atoms, alkoxyalkyl having 1 or 2 carbon atoms in the alkoxy moiety and 1 to 4 carbon atoms in the alkyl moiety, alkenyl having 2 to 5 carbon atoms, alkynyl having 2 to 5 carbon atoms or benzyl. X^1 preferably represents chlorine, bromine, iodine or the radical of the formula $R^{10}O{-}SO_2{-}O$, in which R^{10} has the meanings given above as being preferred.

Particular preference is given to those compounds of the formula (IV) in which

R^{10} represents methyl, ethyl, propyl, methoxymethyl, methoxyethyl, alkenyl having 3 or 4 carbon atoms, alkynyl having 3 or 4 carbon atoms or benzyl and

X^1 represents chlorine, bromine, iodine or the radical of the formula $R^{10}O{-}SO_2{-}O$, in which R^{10} has the meanings given above as being particularly preferred.

The compounds of the formula (IV) are known or can be prepared by known methods.

If the reducing agent used for carrying out the first step of the process (a, variant α) according to the invention is diisobutylaluminum hydride, the process is preferably carried out under the conditions already mentioned in connection with the description of the process (c, variant α).

If the reducing agent used for carrying out the first step of the process (a, variant α) according to the invention is sodium borohydride, the diluents used are generally alcohols, preferably methanol, ethanol or isopropanol.

In the reduction with sodium borohydride, the reaction temperatures can be varied within a certain range. In general, the process is carried out at temperatures between 0°C and 70°C, preferably between 0°C and 50°C.

When carrying out the reduction with sodium borohydride, an equivalent amount or else an excess of sodium borohydride is employed per mole of pyrazolopyrimidine of the formula (II). Work-up is again carried out by customary methods.

The process (a, variant β) according to the invention is generally carried out under the conditions which have already been mentioned in connection with the description of the process (c, variant β).

Suitable diluents for carrying out the second step of the process (a) according to the invention are all customary inert organic solvents. Preference is given to using ethers, such as dioxane or tetrahydrofuran, and furthermore nitriles, such as acetonitrile.

When carrying out the second step of the process (a) according to the invention, the temperatures can be varied within a relatively wide range. In general, the process is carried out at temperatures between 0°C and 100°C, preferably between 20°C and 80°C.

When carrying out the second step of the process (a) according to the invention, in general from 1 to 2 mol, preferably from 1 to 1.5 mol, of the compound of the formula (IV) are employed per mole of pyrazolopyrimidine of the formula (Ia). Work-up is again carried out by customary methods.

The formula (Ia) provides a general definition of the pyrazolopyrimidines required as starting materials for carrying out the process (b) according to the invention. In this formula, R^1, R^2, R^3, R^4, R^7 and R^8 preferably have those meanings which have already been mentioned in connection with the description of the compounds of the formula (I) according to the invention as being preferred for these radicals.

The pyrazolopyrimidines of the formula (Ia) are compounds according to the invention which can be prepared by the process (a) according to the invention.

The formula (V) provides a definition of the diols required as reaction components for carrying out the process (b) according to the invention. Preference is given to diols of the formula (V) in which

p represents 2, 3 or 4 and

1 or 2 hydrogen atoms may be replaced by methyl, ethyl, hydroxy, methoxy, ethoxy, hydroxymethyl, methoxymethyl or ethoxymethyl.

Particular preference is given to diols of the formula (V) in which

p represents 2 and

1 or 2 hydrogen atoms may be replaced by methyl, ethyl, hydroxy, methoxy, ethoxy, hydroxymethyl, methoxymethyl or ethoxymethyl.

Suitable catalysts for carrying out the process (b) according to the invention are all reaction promoters customary for such reactions. Preference is given to using acidic catalysts, such as dilute hydrochloric acid or dilute sulfuric acid, furthermore p-toluene sulfonic acid.

Suitable for use as diluents for carrying out the process (b) according to the invention are all customary inert organic solvents. Preference is given to using ethers, such as diethyl ether, tetrahydrofuran or dioxane, nitriles, such as acetonitrile, or aromatic hydrocarbons, such as toluene. Moreover, the diols for their part may also act as solvents.

When carrying out the process (b) according to the invention, the temperatures can be varied within a certain range. In general, the process is carried out at temperatures between 0°C and 150°C, preferably between 20°C and 120°C.

When carrying out the process (b) according to the invention, in general an excess of diol of the formula (V) is employed per mole of pyrazolopyrimidine of the formula (Ia). Work-up is carried out by customary methods.

The compounds according to the invention have potent microbicidal activity and can be employed for controlling unwanted microorganisms, such as fungi and bacteria, in crop protection and in the protection of materials.

Fungicides can be employed in crop protection for controlling Plasmodiophoromycetes, Oomycetes, Chytridiomycetes, Zygomycetes, Ascomycetes, Basidiomycetes and Deuteromycetes.

Bactericides can be employed in crop protection for controlling Pseudomonadaceae, Rhizobiaceae, Enterobacteriaceae, Corynebacteriaceae and Streptomycetaceae.

Some pathogens causing fungal and bacterial diseases which come under the generic names listed above may be mentioned as examples, but not by way of limitation:

Xanthomonas species, such as, for example, Xanthomonas campestris pv. oryzae;
Pseudomonas species, such as, for example, Pseudomonas syringae pv. lachrymans;
Erwinia species, such as, for example, Erwinia amylovora;
Pythium species, such as, for example, Pythium ultimum;
Phytophthora species, such as, for example, Phytophthora infestans;

Pseudoperonospora species, such as, for example, Pseudoperonospora humuli or Pseudoperonospora cubensis;
Plasmopara species, such as, for example, Plasmopara viticola;
Bremia species, such as, for example, Bremia lactucae;
Peronospora species, such as, for example, Peronospora pisi or P. brassicae;
Erysiphe species, such as, for example, Erysiphe graminis;
Sphaerotheca species, such as, for example, Sphaerotheca fuliginea;
Podosphaera species, such as, for example, Podosphaera leucotricha;
Venturia species, such as, for example, Venturia inaequalis;
Pyrenophora species, such as, for example, Pyrenophora teres or P. graminea (conidia form: Drechslera, syn: Helminthosporium);
Cochliobolus species, such as, for example, Cochliobolus sativus (conidia form: Drechslera, syn: Helminthosporium);
Uromyces species, such as, for example, Uromyces appendiculatus;
Puccinia species, such as, for example, Puccinia recondita;
Sclerotinia species, such as, for example, Sclerotinia sclerotiorum;
Tilletia species, such as, for example, Tilletia caries;
Ustilago species, such as, for example, Ustilago nuda or Ustilago avenae;
Pellicularia species, such as, for example, Pellicularia sasakii;
Pyricularia species, such as, for example, Pyricularia oryzae;
Fusarium species, such as, for example, Fusarium culmorum;
Botrytis species, such as, for example, Botrytis cinerea;
Septoria species, such as, for example, Septoria nodorum;
Leptosphaeria species, such as, for example, Leptosphaeria nodorum;
Cercospora species, such as, for example, Cercospora canescens;
Alternaria species, such as, for example, Alternaria brassicae; and
Pseudocercosporella species, such as, for example, Pseudocercosporella herpotrichoides.

The active compounds according to the invention also show a strong invigorating action in plants. Accordingly, they are suitable for mobilizing the internal defenses of the plant against attack by unwanted microorganisms.

In the present context, plant-invigorating (resistance-inducing) compounds are to be understood as meaning substances which are capable of stimulating the defense system of plants such that, when the treated plants are subsequently inoculated with unwanted microorganisms, they display substantial resistance to these microorganisms.

In the present case, unwanted microorganisms are to be understood as meaning phytopathogenic fungi, bacteria and viruses. The compounds according to the invention can thus be used to protect plants within a certain period of time after treatment against attack by the pathogens mentioned. The period of time for which this protection is achieved generally extends for 1 to 10 days, preferably 1 to 7 days, from the treatment of the plants with the active compounds.

The fact that the active compounds are well tolerated by plants at the concentrations required for controlling plant diseases permits the treatment of above-ground parts of plants, of propagation stock and seeds, and of the soil.

The active compounds according to the invention can be employed with particularly good results for controlling cereal diseases, such as, for example, against Erysiphe species, and diseases in viticulture and in the cultivation of fruit and vegetables, such as, for example, against Botrytis, Venturia, Sphaerotheca and Podosphaeva species.

The active compounds according to the invention are also suitable for increasing the yield of crops. In addition, they show reduced toxicity and are well tolerated by plants.

If appropriate, the active compounds according to the invention can, at certain concentrations and application rates, also be employed as herbicides, for regulating plant growth and for controlling animal pests. If appropriate, they can also be used as intermediates or precursors in the synthesis of other active compounds.

According to the invention, it is possible to treat all plants and parts of plants. Plants are to be understood here as meaning all plants and plant populations, such as desired and undesired wild plants or crop plants (including naturally occurring crop plants). Crop plants can be plants which can be obtained by conventional breeding and optimization methods or by biotechnological and genetic engineering methods or combinations of these methods, including the transgenic plants and including plant cultivars which can or cannot be protected by plant breeders' certificates. Parts of plants are to be understood as meaning all above-ground and below-ground parts and organs of plants, such as shoot, leaf, flower and root, examples which may be mentioned being leaves, needles, stems, trunks, flowers, fruit-bodies, fruits and seeds and also roots, tubers and rhizomes. Parts of plants also include harvested material and vegetative and generative propagation material, for example seedlings, tubers, rhizomes, cuttings and seeds.

The treatment of the plants and parts of plants according to the invention with the active compounds is carried out directly or by action on their environment, habitat or storage area according to customary treatment methods, for example by dipping, spraying, evaporating,

atomizing, broadcasting, brushing-on and, in the case of propagation material, in particular in the case of seeds, furthermore by one- or multilayer coating.

In the protection of materials, the compounds according to the invention can be employed for protecting industrial materials against infection with, and destruction by, unwanted microorganisms.

Industrial materials in the present context are understood as meaning non-living materials which have been prepared for use in industry. For example, industrial materials which are intended to be protected by active compounds according to the invention from microbial change or destruction can be adhesive, sizes, paper and board, textiles, leather, wood, paints and plastic articles, cooling lubricants and other materials which can be infected with, or destroyed by, microorganisms. Parts of production plants, for example cooling-water circuits, which may be impaired by the proliferation of microorganisms may also be mentioned within the scope of the materials to be protected. Industrial materials which may be mentioned within the scope of the present invention are preferably adhesives, sizes, paper and board, leather, wood, paints, cooling lubricants and heat-transfer liquids, particularly preferably wood.

Microorganisms capable of degrading or changing the industrial materials which may be mentioned are, for example, bacteria, fungi, yeasts, algae and slime organisms. The active compounds according to the invention preferably act against fungi, in particular molds, wood-discoloring and wood-destroying fungi (Basidiomycetes) and against slime organisms and algae.

Microorganisms of the following genera may be mentioned as examples:

Alternaria, such as Alternaria tenuis,
Aspergillus, such as Aspergillus niger,
Chaetomium, such as Chaetomium globosum,
Coniophora, such as Coniophora puetana,
Lentinus, such as Lentinus tigrinus,
Penicillium, such as Penicillium glaucum,
Polyporus, such as Polyporus versicolor,
Aureobasidium, such as Aureobasidium pullulans,
Sclerophoma, such as Sclerophoma pityophila,
Trichoderma, such as Trichoderma viride,
Escherichia, such as Escherichia coli,
Pseudomonas, such as Pseudomonas aeruginosa, and
Staphylococcus, such as Staphylococcus aureus.

Depending on their particular physical and/or chemical properties, the active compounds can be converted into the customary formulations, such as solutions, emulsions, suspensions, powders, foams, pastes, granules, aerosols and microencapsulations in polymeric substances and in coating compositions for seeds, and ULV cool and warm fogging formulations.

These formulations are produced in a known manner, for example by mixing the active compounds with extenders, that is liquid solvents, liquefied gases under pressure, and/or solid carriers, optionally with the use of surfactants, that is emulsifiers and/or dispersants, and/or foam formers. If the extender used is water, it is also possible to employ, for example, organic solvents as auxiliary solvents. Essentially, suitable liquid solvents are: aromatics such as xylene, toluene or alkylnaphthalenes, chlorinated aromatics or chlorinated aliphatic hydrocarbons such as chlorobenzenes, chloroethylenes or methylene chloride, aliphatic hydrocarbons such as cyclohexane or paraffins, for example petroleum fractions, alcohols such as butanol or glycol and their ethers and esters, ketones such as acetone, methyl ethyl ketone, methyl isobutyl ketone or cyclohexanone, strongly polar solvents such as dimethylformamide or dimethyl sulfoxide, or else water. Liquefied gaseous extenders or carriers are to be understood as meaning liquids which are gaseous at standard temperature and under atmospheric pressure, for example aerosol propellants such as halogenated hydrocarbons, or else butane, propane, nitrogen and carbon dioxide. Suitable solid carriers are: for example ground natural minerals such as kaolins, clays, talc, chalk, quartz, attapulgite, montmorillonite or diatomaceous earth, and ground synthetic minerals such as finely divided silica, alumina and silicates. Suitable solid carriers for granules are: for example crushed and fractionated natural rocks such as calcite, pumice, marble, sepiolite and dolomite, or else synthetic granules of inorganic and organic meals, and granules of organic material such as sawdust, coconut shells, maize cobs and tobacco stalks. Suitable emulsifiers and/or foam formers are: for example nonionic and anionic emulsifiers, such as polyoxyethylene fatty acid esters, polyoxyethylene fatty alcohol ethers, for example alkylaryl polyglycol ethers, alkylsulfonates, alkyl sulfates, arylsulfonates, or else protein hydrolyzates. Suitable dispersants are: for example lignosulfite waste liquors and methylcellulose.

Tackifiers such as carboxymethylcellulose, natural and synthetic polymers in the form of powders, granules or latices, such as gum arabic, polyvinyl alcohol and polyvinyl acetate, or else natural phospholipids such as cephalins and lecithins and synthetic phospholipids can be used in the formulations. Other possible additives are mineral and vegetable oils.

It is possible to use colorants such as inorganic pigments, for example iron oxide, titanium oxide and Prussian Blue, and organic dyestuffs such as alizarin dyestuffs, azo dyestuffs and metal

phthalocyanine dyestuffs, and trace nutrients such as salts of iron, manganese, boron, copper, cobalt, molybdenum and zinc.

The formulations generally comprise between 0.1 and 95 percent by weight of active compound, preferably between 0.5 and 90%.

The active compounds according to the invention can, as such or in their formulations, also be used in a mixture with known fungicides, bactericides, acaricides, nematicides or insecticides, to broaden, for example, the activity spectrum or to prevent development of resistance. In many cases, synergistic effects are obtained, i.e. the activity of the mixture is greater than the activity of the individual components.

Suitable mixing components are, for example, the following compounds:

Fungicides:

2-phenylphenol; 8-hydroxyquinoline sulfate; acibenzolar-S-methyl; aldimorph; amidoflumet; ampropylfos; ampropylfos-potassium; andoprim; anilazine; azaconazole; azoxystrobin; benalaxyl; benalaxyl-M, benodanil; benomyl; benthiavalicarb-isopropyl; benzamacril; benzamacril-isobutyl; bilanafos; binapacryl; biphenyl; bitertanol; blasticidin-S; boscalid; bromuconazole; bupirimate; buthiobate; butylamine; calcium polysulfide; capsimycin; captafol; captan; carbendazim; carboxin; carpropamid; carvone; chinomethionat; chlobenthiazone; chlorfenazole; chloroneb; chlorothalonil; chlozolinate; clozylacon; cyazofamid; cyflufenamid; cymoxanil; cyproconazole; cyprodinil; cyprofuram; Dagger G; debacarb; dichlofluanid; dichlone; dichlorophen; diclocymet; diclomezine; dicloran; diethofencarb; difenoconazole; diflumetorim; dimethirimol; dimethomorph; dimoxystrobin; diniconazole; diniconazole-M; dinocap; diphenylamine; dipyrithione; ditalimfos; dithianon; dodine; drazoxolon; edifenphos; epoxiconazole; ethaboxam; ethirimol; etridiazole; famoxadone; fenamidone; fenapanil; fenarimol; fenbuconazole; fenfuram; fenhexamid; fenitropan; fenoxanil; fenpiclonil; fenpropidin; fenpropimorph; ferbam; fluazinam; flubenzimine; fludioxonil; flumetover; flumorph; fluoromide; fluoxastrobin; fluquinconazole; flurprimidol; flusilazole; flusulfamide; flutolanil; flutriafol; folpet; fosetyl-Al; fosetyl-sodium; fuberidazole; furalaxyl; furametpyr; furcarbanil; furmecyclox; guazatine; hexachlorobenzene; hexaconazole; hymexazole; imazalil; imibenconazole; iminoctadine triacetate; iminoctadine tris(albesilate); iodocarb; ipconazole; iprobenfos; iprodione; iprovalicarb; irumamycin; isoprothiolane; isovaledione; kasugamycin; kresoxim-methyl; mancozeb; maneb; meferimzone; mepanipyrim; mepronil; metalaxyl; metalaxyl-M; metconazole; methasulfocarb; methfuroxam; metiram; metominostrobin; metsulfovax; mildiomycin; myclobutanil; myclozolin; natamycin; nicobifen; nitrothal-isopropyl; noviflumuron; nuarimol; ofurace; orysastrobin; oxadixyl; oxolinic acid; oxpoconazole;

oxycarboxin; oxyfenthiin; paclobutrazole; pefurazoate; penconazole; pencycuron; phosdiphen; phthalide; picoxystrobin; piperalin; polyoxins; polyoxorim; probenazole; prochloroaz; procymidone; propamocarb; propanosine-sodium; propiconazole; propineb; proquinazid; prothioconazole; pyraclostrobin; pyrazophos; pyrifenox; pyrimethanil; pyroquilon; pyroxyfur; pyrrolenitrine; quinconazole; quinoxyfen; quintozene; simeconazole; spiroxamine; sulfur; tebuconazole; tecloftalam; tecnazene; tetcyclacis; tetraconazole; thiabendazole; thicyofen; thifluzamide; thiophanate-methyl; thiram; tioxymid; tolclofos-methyl; tolylfluanid; triadimefon; triadimenol; triazbutil; triazoxide; tricyclamide; tricyclazole; tridemorph; trifloxystrobin; triflumizole; triforine; triticonazole; uniconazole; validamycin A; vinclozolin; zineb; ziram; zoxamide; (2S)-N-[2-[4-[[3-(4-chlorophenyl)-2-propynyl]oxy]-3-methoxyphenyl]ethyl]-3-methyl-2-[(methylsulfonyl)amino]butanamide; 1-(1-naphthalenyl)-1H-pyrrole-2,5-dione; 2,3,5,6-tetrachloro-4-(methylsulfonyl)pyridine; 2-amino-4-methyl-N-phenyl-5-thiazolecarboxamide; 2-chloro-N-(2,3-dihydro-1,1,3-trimethyl-1H-inden-4-yl)-3-pyridinecarboxamide; 3,4,5-trichloro-2,6-pyridinedicarbonitrile; actinovate; cis-1-(4-chlorophenyl)-2-(1H-1,2,4-triazol-1-yl)cycloheptanol; methyl 1-(2,3-dihydro-2,2-dimethyl-1H-inden-1-yl)-1H-imidazole-5-carboxylate; monopotassium carbonate; N-(6-methoxy-3-pyridinyl)cyclopropanecarboxamide; N-butyl-8-(1,1-dimethylethyl)-1-oxaspiro[4.5]decane-3-amine; sodium tetracarbonate;

and copper salts and preparations, such as Bordeaux mixture; copper hydroxide; copper naphthenate; copper oxychloride; copper sulfate; cufraneb; copper oxide; mancopper; oxine-copper.

Bactericides:

bronopol, dichlorophen, nitrapyrin, nickel dimethyldithiocarbamate, kasugamycin, octhilinone, furancarboxylic acid, oxytetracyclin, probenazole, streptomycin, tecloftalam, copper sulfate and other copper preparations.

Insecticides/acaricides/nematicides:

1. Acetylcholinesterase (AChE) inhibitors

1.1 carbamates (for example alanycarb, aldicarb, aldoxycarb, allyxycarb, aminocarb, azamethiphos, bendiocarb, benfuracarb, bufencarb, butacarb, butocarboxim, butoxycarboxim, carbaryl, carbofuran, carbosulfan, chloethocarb, coumaphos, cyanofenphos, cyanophos, dimetilan, ethiofencarb, fenobucarb, fenothiocarb, formetanate, furathiocarb, isoprocarb, metam-sodium,

methiocarb, methomyl, metolcarb, oxamyl, pirimicarb, promecarb, propoxur, thiodicarb, thiofanox, triazamate, trimethacarb, XMC, xylylcarb)

1.2 organophosphates (for example acephate, azamethiphos, azinphos (-methyl, -ethyl), bromophos-ethyl, bromfenvinfos (-methyl), butathiofos, cadusafos, carbophenothion, chlorethoxyfos, chlorfenvinphos, chlormephos, chlorpyrifos (-methyl/-ethyl), coumaphos, cyanofenphos, cyanophos, chlorofenvinphos, demeton-s-methyl, demeton-S-methylsulfone, dialifos, diazinon, dichlofenthion, dichlorvos/DDVP, dicrotophos, dimethoate, dimethylvinphos, dioxabenzofos, disulfoton, EPN, ethion, ethoprophos, etrimfos, famphur, fenamiphos, fenitrothion, fensulfothion, fenthion, flupyrazofos, fonofos, formothion, fosmethilan, fosthiazate, heptenophos, iodofenphos, iprobenfos, isazofos, isofenphos, isopropyl o-salicylate, isoxathion, malathion, mecarbam, methacrifos, methamidophos, methidathion, mevinphos, monocrotophos, naled, omethoate, oxydemeton-methyl, parathion (-methyl/-ethyl), phenthoate, phorate, phosalone, phosmet, phosphamidon, phosphocarb, phoxim, pirimiphos (-methyl/-ethyl), profenofos, propaphos, propetamphos, prothiofos, prothoate, pyraclofos, pyridaphenthion, pyridathion, quinalphos, sebufos, sulfotep, sulprofos, tebupirimfos, temephos, terbufos, tetrachlorovinphos, thiometon, triazophos, triclorfon, vamidothion)

2. Sodium channel modulators/blockers of voltage-gated sodium channels

2.1 pyrethroids (for example acrinathrin, allethrin (d-cis-trans, d-trans), beta-cyfluthrin, bifenthrin, bioallethrin, bioallethrin-S-cyclopentyl-isomer, bioethanomethrin, biopermethrin, bioresmethrin, chlovaporthrin, cis-cypermethrin, cis-resmethrin, cis-permethrin, clocythrin, cycloprothrin, cyfluthrin, cyhalothrin, cypermethrin (alpha-, beta-, theta-, zeta-), cyphenothrin, DDT, deltamethrin, empenthrin (1R-isomer), esfenvalerate, etofenprox, fenfluthrin, fenpropathrin, fenpyrithrin, fenvalerate, flubrocythrinate, flucythrinate, flufenprox, flumethrin, fluvalinate, fubfenprox, gamma-cyhalothrin, imiprothrin, kadethrin, lambda-cyhalothrin, metofluthrin, permethrin (cis-, trans-), phenothrin (1R-trans isomer), prallethrin, profluthrin, protrifenbute, pyresmethrin, resmethrin, RU 15525, silafluofen, tau-fluvalinate, tefluthrin, terallethrin, tetramethrin (1R-isomer), tralomethrin, transfluthrin, ZXI 8901, pyrethrins (pyrethrum))

2.2 oxadiazines (for example indoxacarb)

3. Acetylcholine receptor agonists/antagonists

3.1 chloronicotinyls/neonicotinoids (for example acetamiprid, clothianidin, dinotefuran, imidacloprid, nitenpyram, nithiazine, thiacloprid, thiamethoxam)

3.2 nicotine, bensultap, cartap

4. Acetylcholine receptor modulators

4.1 spinosyns (for example spinosad)

5. Antagonists of GABA-gated chloride channels

5.1 cyclodiene organochlorines (for example camphechloro, chlorodane, endosulfan, gamma-HCH, HCH, heptachloro, lindane, methoxychloro

5.2 fiproles (for example acetoprole, ethiprole, fipronil, vaniliprole)

6. Chloride channel activators

6.1 mectins (for example abamectin, avermectin, emamectin, emamectin-benzoate, ivermectin, milbemectin, milbemycin)

7. Juvenile hormone mimetics

(for example diofenolan, epofenonane, fenoxycarb, hydroprene, kinoprene, methoprene, pyriproxifen, triprene)

8. Ecdyson agonists/disruptors

8.1 diacylhydrazines (for example chromafenozide, halofenozide, methoxyfenozide, tebufenozide)

9. Chitin biosynthesis inhibitors

9.1 benzoylureas (for example bistrifluron, chlofluazuron, diflubenzuron, fluazuron, flucycloxuron, flufenoxuron, hexaflumuron, lufenuron, novaluron, noviflumuron, penfluron, teflubenzuron, triflumuron)

9.2 buprofezin

9.3 cyromazine

10. Inhibitors of oxidative phosphorylation, ATP disruptors

10.1 diafenthiuron

10.2 organotins (for example azocyclotin, cyhexatin, fenbutatin-oxide)

11. Decouplers of oxidative phosphorylation acting by interrupting the H-proton gradient

11.1 pyrroles (for example chlorfenapyr)

11.2 dinitrophenols (for example binapacryl, dinobuton, dinocap, DNOC)

12. Site-I electron transport inhibitors

12.1 METIs (for example fenazaquin, fenpyroximate, pyrimidifen, pyridaben, tebufenpyrad, tolfenpyrad)

12.2 hydramethylnone

12.3 dicofol

13. Site-II electron transport inhibitors

13.1 rotenone

14. Site-III electron transport inhibitors

14.1 acequinocyl, fluacrypyrim

15. Microbial disruptors of the insect gut membrane

Bacillus thuringiensis strains

16. Inhibitors of fat synthesis

16.1 tetronic acids (for example spirodiclofen, spiromesifen)

16.2 tetramic acids [for example 3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl carbonate (alias: carbonic acid, 3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl ester, CAS Reg. No.: 382608-10-8) and carbonic acid, cis-3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl ester (CAS Reg. No.: 203313-25-1)]

17. Carboxamides

(for example flonicamid)

18. Octopaminergic agonists

(for example amitraz)

19. Inhibitors of magnesium-stimulated ATPase

(for example propargite)

20. Phthalamides

(for example N^2-[1,1-dimethyl-2-(methylsulfonyl)ethyl]-3-iodo-N^1-[2-methyl-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl]phenyl]-1,2-benzenedicarboxamide (CAS Reg. No.: 272451-65-7), flubendiamide)

21. Nereistoxin analogues

(for example thiocyclam hydrogen oxalate, thiosultap-sodium)

22. Biologicals, hormones or pheromones

(for example azadirachtin, Bacillus spec., Beauveria spec., codlemone, Metarrhizium spec., Paecilomyces spec., thuringiensin, Verticillium spec.)

23. Active compounds with unknown or unspecific mechanisms of action

23.1 fumigants (for example aluminum phosphide, methyl bromide, sulfuryl fluoride)

23.2 selective antifeedants (for example cryolite, flonicamid, pymetrozine)

23.3 mite growth inhibitors (for example clofentezine, etoxazole, hexythiazox)

23.4 amidoflumet, benclothiaz, benzoximate, bifenazate, bromopropylate, buprofezin, chinomethionat, chlordimeform, chlorobenzilate, chloropicrin, clothiazoben, cycloprene, cyflumetofen, dicyclanil, fenoxacrim, fentrifanil, flubenzimine, flufenerim, flutenzin, gossyplure, hydramethylnone, japonilure, metoxadiazone, petroleum, piperonyl butoxide, potassium oleate, pyrafluprole, pyridalyl, pyriprole, sulfluramid, tetradifon, tetrasul, triarathene, verbutin,

furthermore the compound 3-methylphenyl propylcarbamate (Tsumacide Z), the compound 3-(5-chloro-3-pyridinyl)-8-(2,2,2-trifluoroethyl)-8-azabicyclo[3.2.1]octane-3-carbonitrile (CAS Reg. No. 185982-80-3) and the corresponding 3-endo-isomer (CAS Reg. No. 185984-60-5) (cf. WO 96/37494, WO 98/25923), and preparations which comprise insecticidally active plant extracts, nematodes, fungi or viruses.

A mixture with other known active compounds, such as herbicides, or with fertilizers and growth regulators, safeners and/or semiochemicals is also possible.

In addition, the compounds of the formula (I) according to the invention also have very good antimycotic activity. They have a very broad antimycotic activity spectrum in particular against dermatophytes and yeasts, molds and diphasic fungi (for example against Candida species such as Candida albicans, Candida glabrata) and Epidermophyton floccosum, Aspergillus species such as Aspergillus niger and Aspergillus fumigatus, Trichophyton species such as Trichophyton mentagrophytes, Microsporon species such as Microsporon canis and audouinii. The list of these fungi does by no means limit the mycotic spectrum which can be covered, but is only for illustration.

The active compounds can be used as such, in the form of their formulations or the use forms prepared therefrom, such as ready-to-use solutions, suspensions, wettable powders, pastes, soluble powders, dusts and granules. Application is carried out in a customary manner, for example by watering, spraying, atomizing, broadcasting, dusting, foaming, spreading, etc. It is furthermore possible to apply the active compounds by the ultra-low volume method, or to inject the active compound preparation or the active compound itself into the soil. It is also possible to treat the seeds of the plants.

When using the active compounds according to the invention as fungicides, the application rates can be varied within a relatively wide range, depending on the kind of application. For the treatment of parts of plants, the active compound application rates are generally between 0.1 and 10 000 g/ha, preferably between 10 and 1000 g/ha. For seed dressing, the active compound application rates are generally between 0.001 and 50 g per kilogram of seed, preferably between 0.01 and 10 g per kilogram of seed. For the treatment of the soil, the active compound application rates are generally between 0.1 and 10 000 g/ha, preferably between 1 and 5000 g/ha.

As already mentioned above, it is possible to treat all plants and their parts according to the invention. In a preferred embodiment, wild plant species and plant cultivars, or those obtained by conventional biological breeding, such as crossing or protoplast fusion, and parts thereof, are treated. In a further preferred embodiment, transgenic plants and plant cultivars obtained by genetic engineering, if appropriate in combination with conventional methods (Genetically Modified Organisms), and parts thereof, are treated. The term "parts" or "parts of plants" or "plant parts" has been explained above.

Particularly preferably, plants of the plant cultivars which are in each case commercially available or in use are treated according to the invention. Plant cultivars are to be understood as meaning plants having new properties ("traits") and which have been obtained by conventional breeding, by mutagenesis or by recombinant DNA techniques. They can be cultivars, varieties, bio- or genotypes.

Depending on the plant species or plant cultivars, their location and growth conditions (soils, climate, vegetation period, diet), the treatment according to the invention may also result in superadditive ("synergistic") effects. Thus, for example, reduced application rates and/or a widening of the activity spectrum and/or an increase in the activity of the substances and compositions which can be used according to the invention, better plant growth, increased tolerance to high or low temperatures, increased tolerance to drought or to water or soil salt content, increased flowering performance, easier harvesting, accelerated maturation, higher harvest yields, better quality and/or a higher nutritional value of the harvested products, better storage stability and/or processability of the harvested products are possible which exceed the effects which were actually to be expected.

The transgenic plants or plant cultivars (i.e. those obtained by genetic engineering) which are preferably to be treated according to the invention include all plants which, in the genetic modification, received genetic material which imparted particularly advantageous useful properties ("traits") to these plants. Examples of such properties are better plant growth, increased tolerance to high or low temperatures, increased tolerance to drought or to water or soil salt content, increased flowering performance, easier harvesting, accelerated maturation, higher harvest yields, better quality and/or a higher nutritional value of the harvested products, better storage stability and/or processability of the harvested products. Further and particularly emphasized examples of such properties are a better defense of the plants against animal and microbial pests, such as against insects, mites, phytopathogenic fungi, bacteria and/or viruses, and also increased tolerance of the plants to certain herbicidally active compounds. Examples of transgenic plants which may be mentioned are the important crop plants, such as cereals (wheat, rice), corn, soy beans, potatoes, cotton, tobacco, oilseed rape and also fruit plants (with the fruits apples, pears, citrus fruits and grapes), and particular emphasis is given to corn, soy beans, potatoes, cotton, tobacco and oilseed rape. Traits that are particularly emphasized are increased defense of the plants against insects, arachnids, nematodes and slugs and snails by toxins formed in the plants, in particular those formed in the plants by the genetic material from Bacillus thuringiensis (for example by the genes CryIA(a), CryIA(b), CryIA(c), CryIIA, CryIIIA, CryIIIB2, Cry9c, Cry2Ab, Cry3Bb and CryIF and also combinations thereof) (hereinbelow referred to as "Bt plants"). Traits that are also particularly emphasized are the increased defense of the plants against fungi, bacteria and viruses by systemic acquired resistance (SAR), systemin, phytoalexins, elicitors and resistance genes and correspondingly expressed proteins and toxins. Traits that are furthermore particularly emphasized are the increased tolerance of the plants to certain herbicidally active compounds, for example imidazolinones, sulfonylureas, glyphosate or phosphinotricin (for example the "PAT" gene). The genes which impart the desired traits in question can also be present in combination with one another in the transgenic plants. Examples of "Bt plants" which may be mentioned are corn

varieties, cotton varieties, soy bean varieties and potato varieties which are sold under the trade names YIELD GARD® (for example corn, cotton, soy beans), KnockOut® (for example corn), StarLink® (for example corn), Bollgard® (cotton), Nucoton® (cotton) and NewLeaf® (potato). Examples of herbicide-tolerant plants which may be mentioned are corn varieties, cotton varieties and soy bean varieties which are sold under the trade names Roundup Ready® (tolerance to glyphosate, for example corn, cotton, soy bean), Liberty Link® (tolerance to phosphinotricin, for example oilseed rape), IMI® (tolerance to imidazolinones) and STS® (tolerance to sulfonylureas, for example corn). Herbicide-resistant plants (plants bred in a conventional manner for herbicide tolerance) which may be mentioned also include the varieties sold under the name Clearfield® (for example corn). Of course, these statements also apply to plant cultivars which have these genetic traits or genetic traits still to be developed, and which will be developed and/or marketed in the future.

The plants listed can be treated according to the invention in a particularly advantageous manner with the compounds of the general formula (I) or the active compound mixtures according to the invention. The preferred ranges stated above for the active compounds or mixtures also apply to the treatment of these plants. Particular emphasis is given to the treatment of plants with the compounds or mixtures specifically mentioned in the present text.

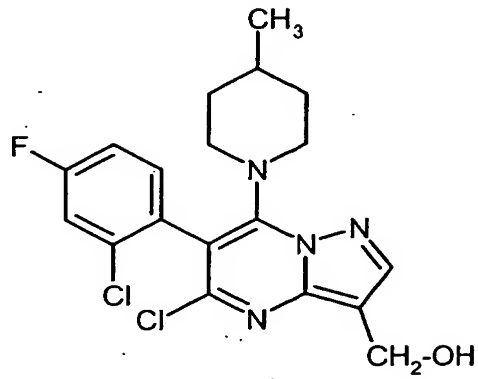
The compounds of the formula (I) according to the invention are furthermore suitable for suppressing the growth of tumour cells in humans and mammals. This is based on an interaction of the compounds according to the invention with tubulin and microtubuli and by promoting microtubuli polymerization.

For this purpose, it is possible to administer an effective amount of one or more compounds of the formula (I) or pharmaceutically acceptable salts thereof.

The preparation and the use of the active compounds according to the invention is illustrated in the examples below.

Preparation examples

Example 1

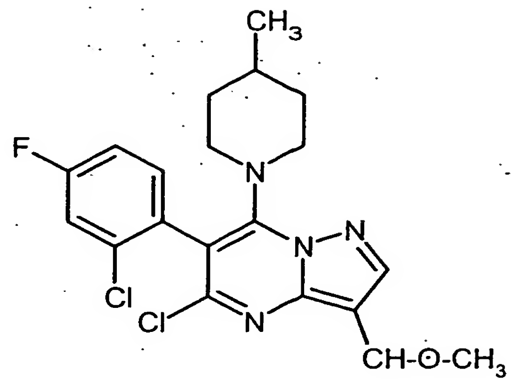


Process (a, variant β):

At room temperature, 0.093 g (2.455 mmol) of sodium borohydride is added a little at a time with stirring to a mixture of 1.0 g (2.455 mmol) of 3-formyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methyl-piperidino)pyrazolo[1,5-a]pyrimidine and 50 ml of methanol. After the evolution of gas has ceased, the mixture is stirred at room temperature for another 2 hours and then concentrated under reduced pressure. The residue that remains is stirred with water and then filtered off with suction and dried. This gives 0.7 g (64.03% of theory) of 3-hydroxymethyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methylpiperidino)pyrazolo[1,5-a]pyrimidine in the form of a colorless solid.

HPLC: logP = 3.89

Example 2

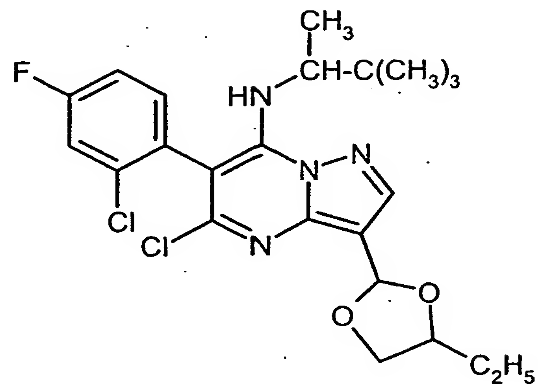


Process (a), second step:

At room temperature, 0.098 g (2.443 mmol) of sodium hydride is added with stirring to a solution of 0.5 g (1.222 mmol) of 3-hydroxymethyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methyl-piperidino)pyrazolo[1,5-a]pyrimidine and 50 ml of tetrahydrofuran. The mixture is allowed to stir at room temperature for another 15 minutes, and 0.191 g (1.344 mmol) of iodomethane is then added. The reaction mixture is stirred at room temperature for 16 hours and then heated at 80°C for 5 hours. Another 0.05 g of sodium hydride and 0.1 g of iodomethane are added, and the mixture is heated under reflux for a further 2 hours. The mixture is then concentrated under reduced pressure and the residue that remains is extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and then concentrated under reduced pressure. The residue that remains is chromatographed on silica gel using a mixture of 4 parts of cyclohexane and 1 part of ethyl acetate. This gives 0.7 g (92.6% of theory) of 3-methoxymethyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methylpiperidno)pyrazolo[1,5-a]pyrimidine.

HPLC: logP = 5.09

Example 23



Process (b):

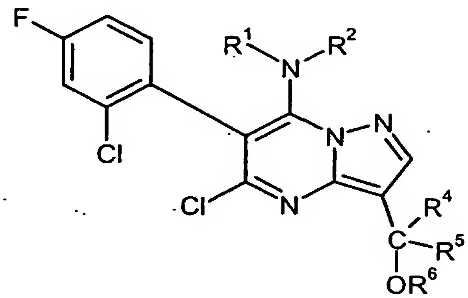
A mixture of 1.22 mmol of 3-formyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(3,3-dimethylbut-2-yl-amino)pyrazolo-[1,5-a]pyrimidine, 1.46 mmol of butane-1,2-diol and 6 mmol of 4-toluenesulfonic acid and 80 ml of toluene is boiled on a water separator for 24 hours. After cooling to room temperature, the organic phase is washed with water and then dried over sodium sulfate and concentrated under reduced pressure. The residue that remains is chromatographed on silica gel. In this manner, the substsance of the formula given above is obtained.

HPLC: log P = 5.70

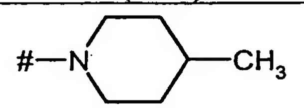
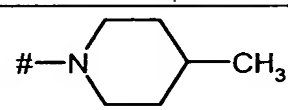
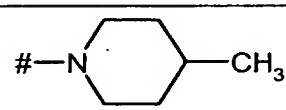
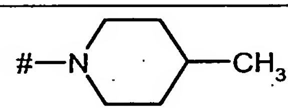
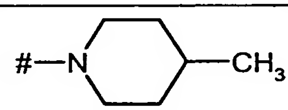
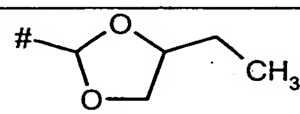
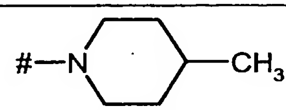
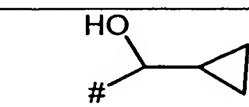
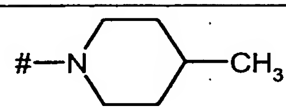
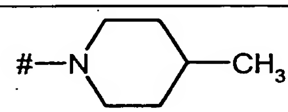
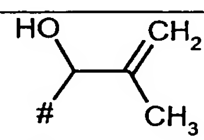
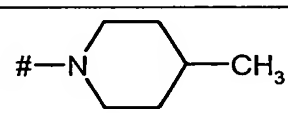
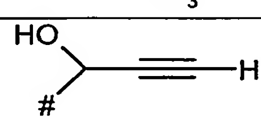
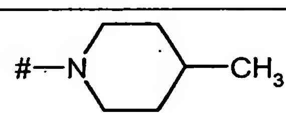
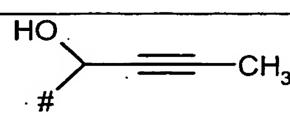
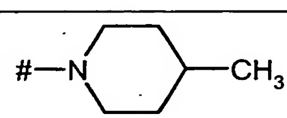
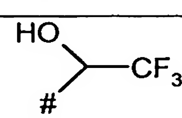
logP value is determined in accordance with EEC Directive 79/831 Annex V. A8 by HPLC (gradient method, acetonitrile/0.1% aqueous phosphoric acid)

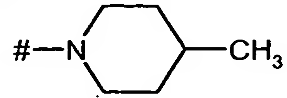
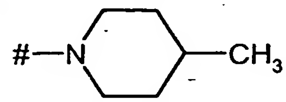
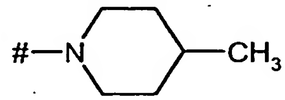
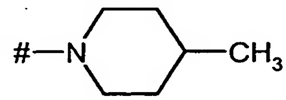
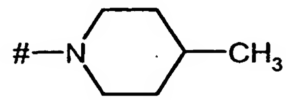
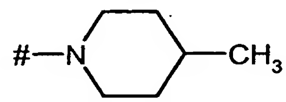
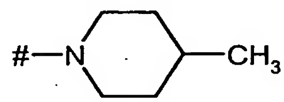
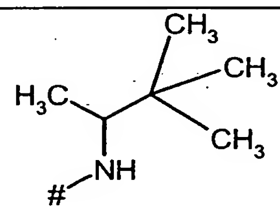
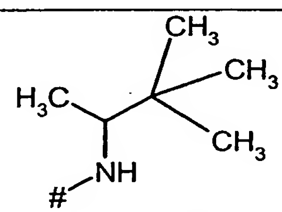
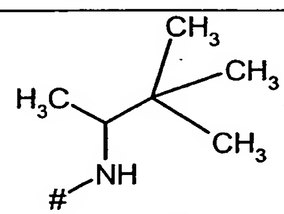
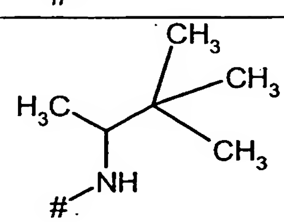
The compounds of the formula (I) listed in tables 1 – 6 below are or were obtained analogously to the methods given above:

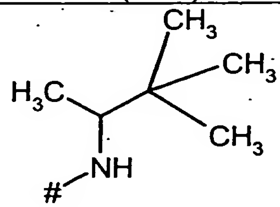
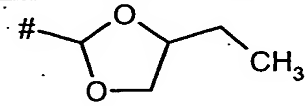
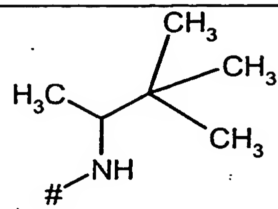
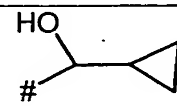
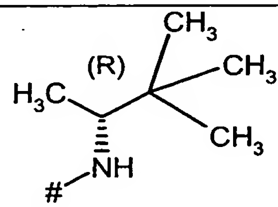
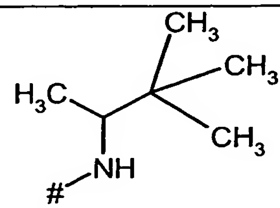
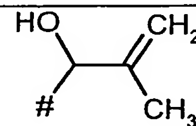
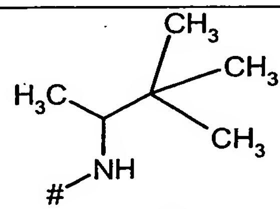
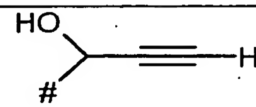
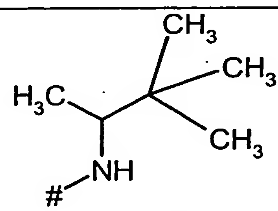
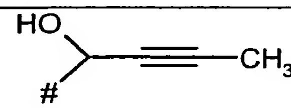
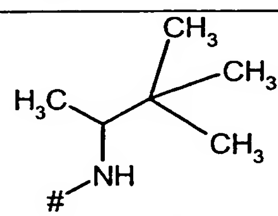
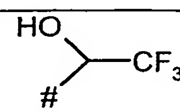
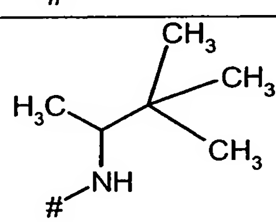
Table 1

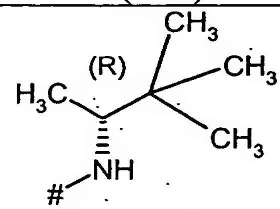
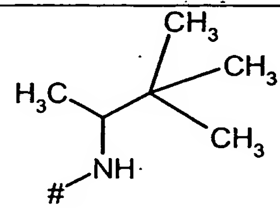
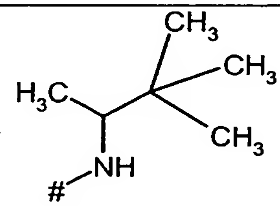
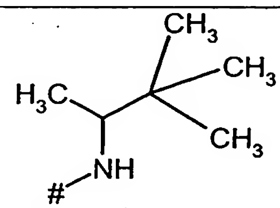
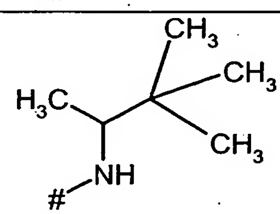
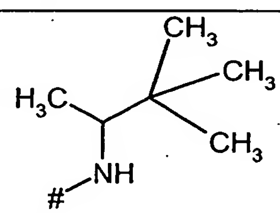
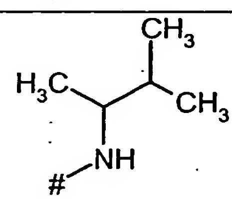
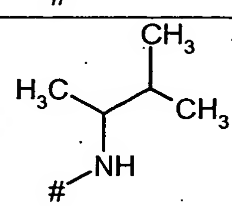


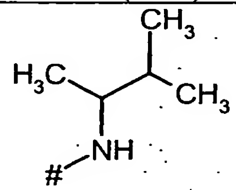
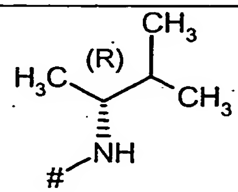
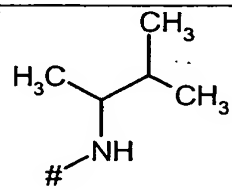
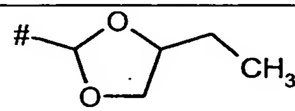
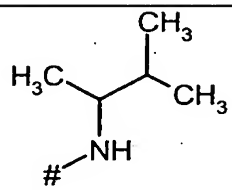
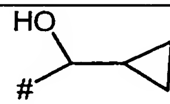
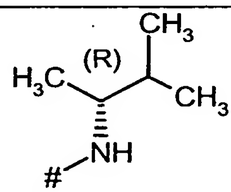
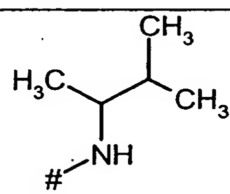
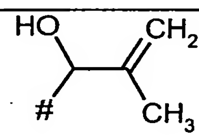
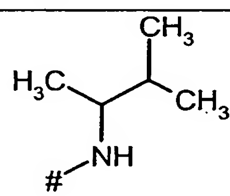
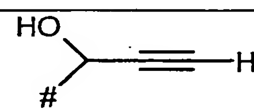
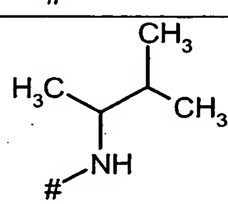
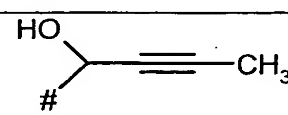
(Ia)

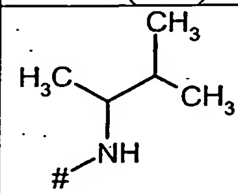
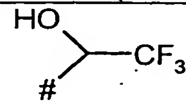
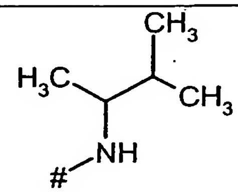
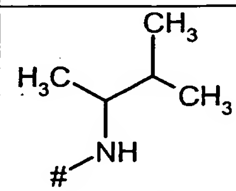
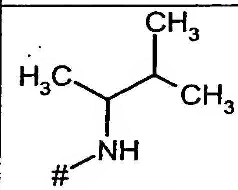
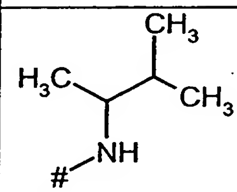
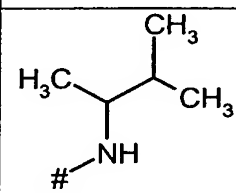
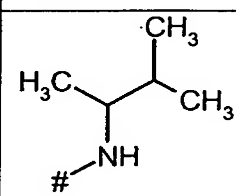
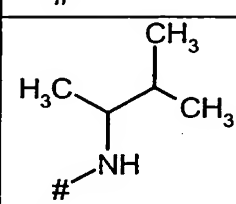
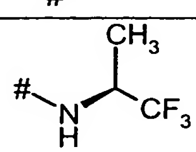
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
1		$-CH_2OH$	3.89
2		$-CH_2-O-CH_3$	5.09
3		allyloxymethyl	5.73
4		$-CH_2-O-C_2H_5$	5.53
5			
6			4.76
7		1-hydroxyethyl	4.24
8			4.74
9			4.38
10			
11			4.99

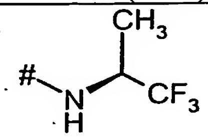
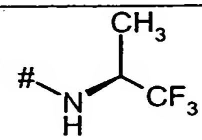
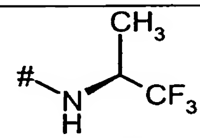
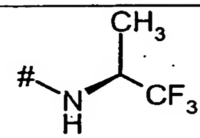
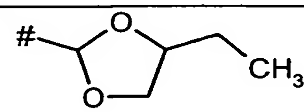
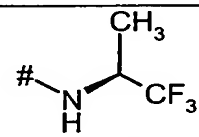
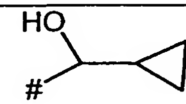
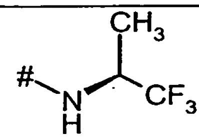
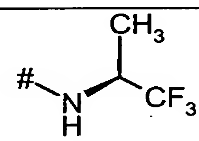
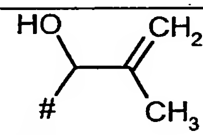
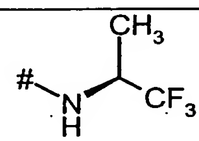
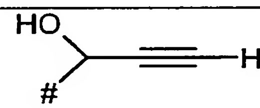
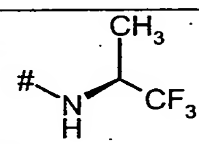
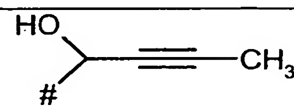
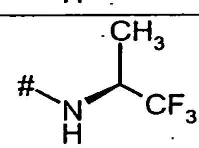
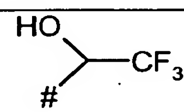
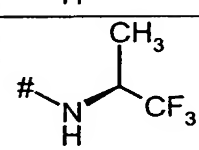
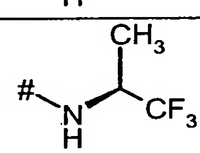
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
12		$-CH(OH)-CH_2Cl$	
13		$-CH(OH)-CH(CH_3)_2$	
14		$-CH(OH)-C(CH_3)_3$	
15		$-C(CH_3)(OH)-CH(CH_3)_2$	
16		$-CH(OCH_3)-CH(CH_3)_2$	
17		$-CH(CH_3)(OCH(CH_3)_2)$	
18		$-C(CH_3)(CF_3)-(OCH_3)$	
19		$-CH_2OH$	3.89
20		$-CH_2-O-CH_3$	
21		allyloxymethyl	
22		$-CH_2-O-C_2H_5$	

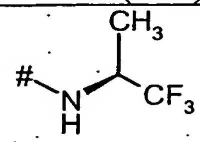
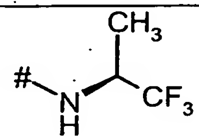
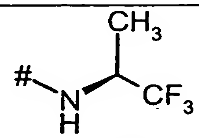
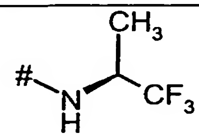
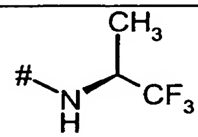
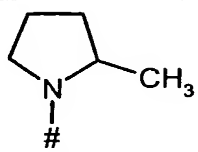
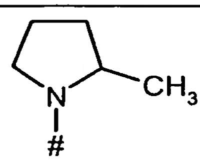
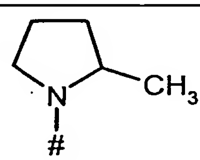
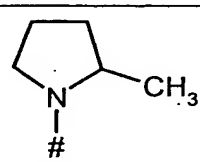
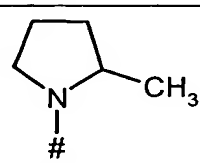
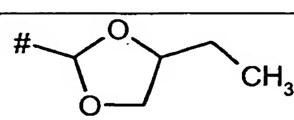
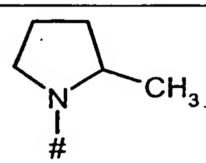
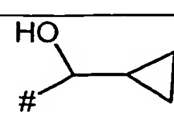
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
23			5.70
24			
25		1-hydroxyethyl	
26			
27			
28			4.54
29			
30		$-CH(OH)-CH_2Cl$	

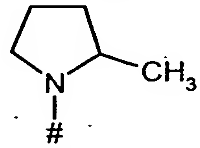
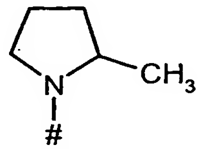
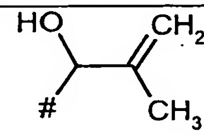
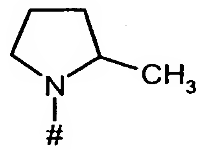
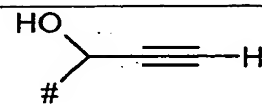
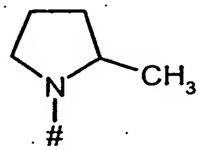
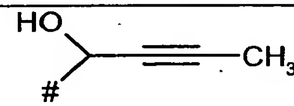
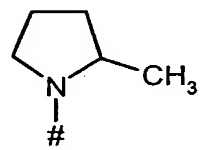
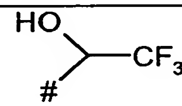
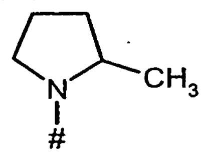
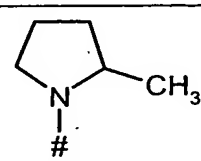
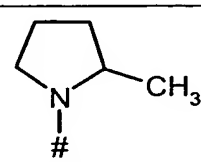
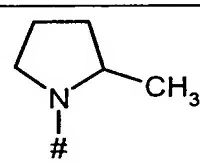
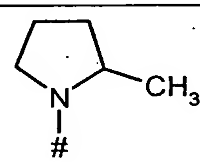
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
31		$-CH(OH)-CH(CH_3)_2$	
32		$-CH(OH)-C(CH_3)_3$	
33		$-C(CH_3)(OH)-CH(CH_3)_2$	
34		$-CH(OCH_3)-CH(CH_3)_2$	
35		$-CH(CH_3)(OCH(CH_3)_2)$	
36		$-C(CH_3)(CF_3)-(OCH_3)$	
37		$-CH_2OH$	3.56
38		$-CH_2-O-CH_3$	4.63

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
39		allyloxymethyl	
40		$-CH_2-O-C_2H_5$	
41			5.70
42			
43		1-hydroxyethyl	
44			
45			
46			4.54

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
47			
48		$-CH(OH)-CH_2Cl$	
49		$-CH(OH)-CH(CH_3)_2$	
50		$-CH(OH)-C(CH_3)_3$	
51		$-C(CH_3)(OH)-CH(CH_3)_2$	
52		$-CH(OCH_3)-CH(CH_3)_2$	
53		$-CH(CH_3)(OCH(CH_3)_2)$	
54		$-C(CH_3)(CF_3)-(OCH_3)$	
55		$-CH_2OH$	3.13

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
56		$-CH_2-O-CH_3$	4.08
57		allyloxymethyl	
58		$-CH_2-O-C_2H_5$	
59			5.70
60			
61		1-hydroxyethyl	
62			
63			
64			4.54
65			
66		$-CH(OH)-CH_2Cl$	
67		$-CH(OH)-CH(CH_3)_2$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
68		$-CH(OH)-C(CH_3)_3$	
69		$-C(CH_3)(OH)-CH(CH_3)_2$	
70		$-CH(OCH_3)-CH(CH_3)_2$	
71		$-CH(CH_3)(OCH(CH_3)_2)$	
72		$-C(CH_3)(CF_3)-(OCH_3)$	
73		$-CH_2OH$	3.34
74		$-CH_2-O-CH_3$	
75		allyloxymethyl	
76		$-CH_2-O-C_2H_5$	
77			5.70
78			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
79		1-hydroxyethyl	
80			
81			
82			4.54
83			
84		$-CH(OH)-CH_2Cl$	
85		$-CH(OH)-CH(CH_3)_2$	
86		$-CH(OH)-C(CH_3)_3$	
87		$-C(CH_3)(OH)-CH(CH_3)_2$	
88		$-CH(OCH_3)-CH(CH_3)_2$	

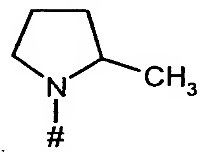
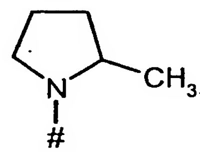
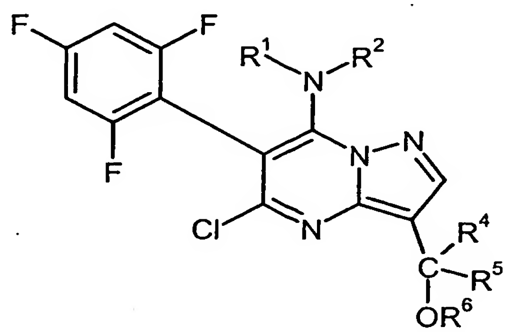
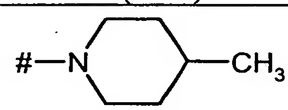
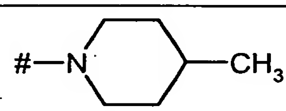
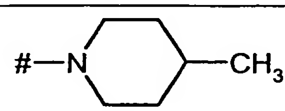
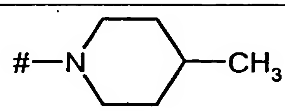
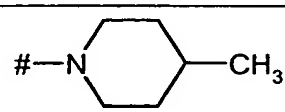
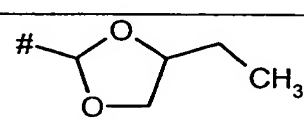
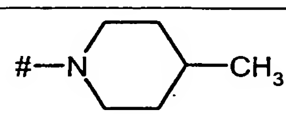
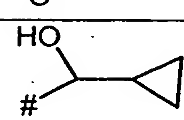
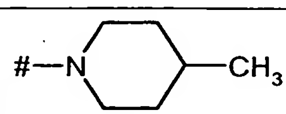
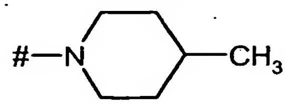
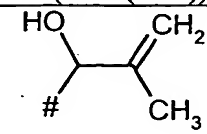
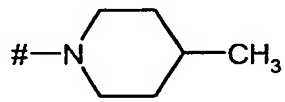
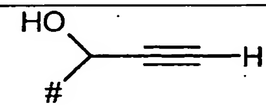
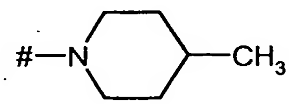
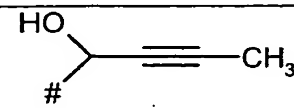
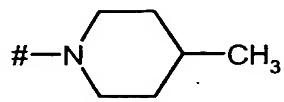
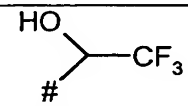
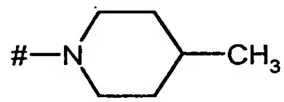
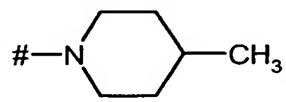
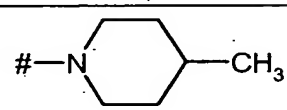
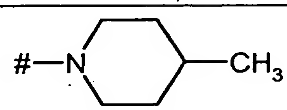
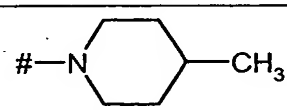
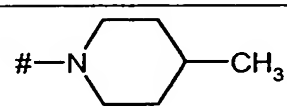
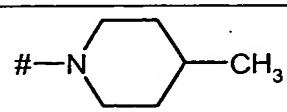
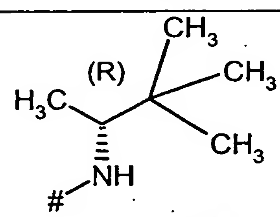
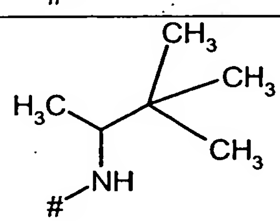
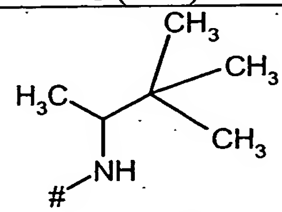
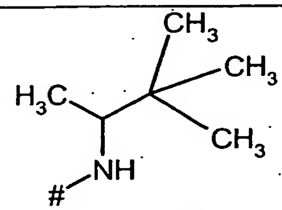
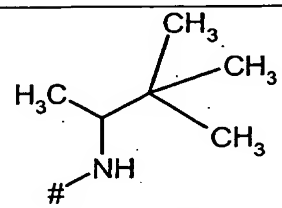
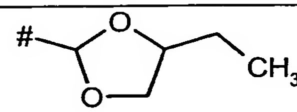
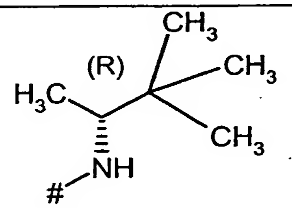
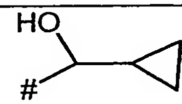
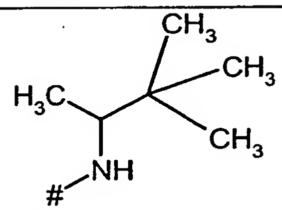
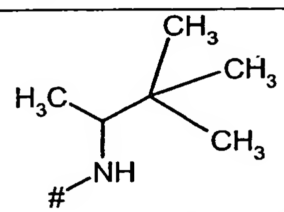
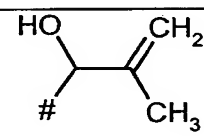
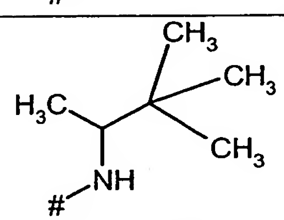
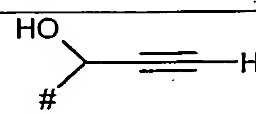
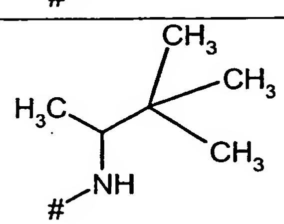
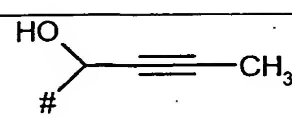
Ex. No.	N(R¹R²)	-C(R⁴R⁵(OR⁶))	logP
89		-CH(CH₃)(OCH(CH₃)₂)	
90		-C(CH₃)(CF₃)-(OCH₃)	

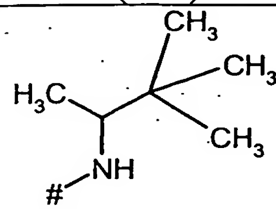
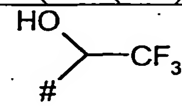
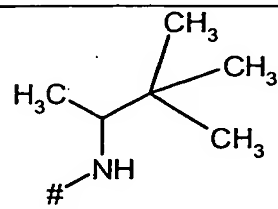
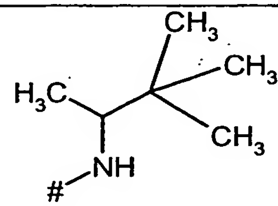
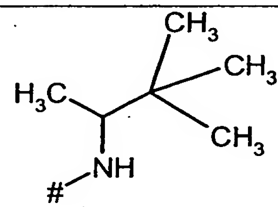
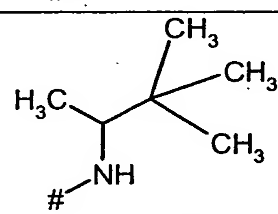
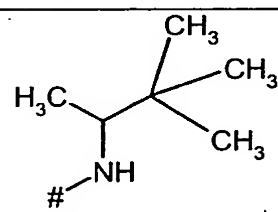
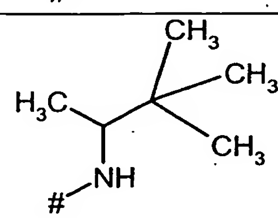
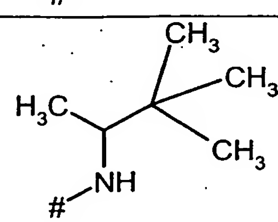
Table 2

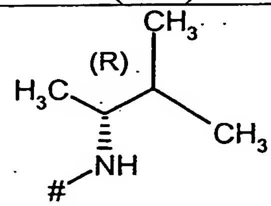
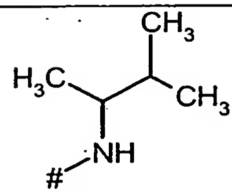
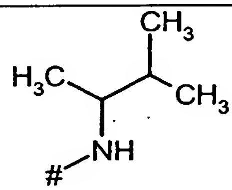
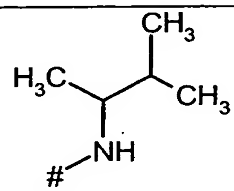
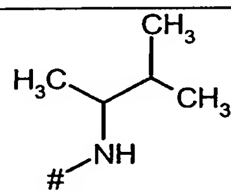
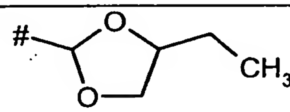
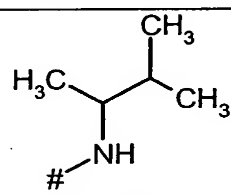
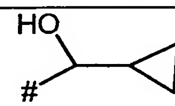
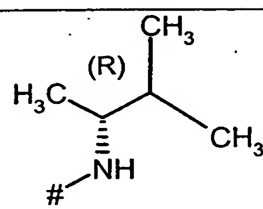
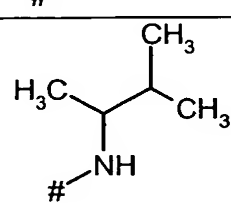
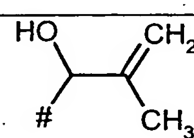


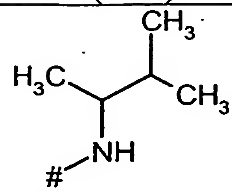
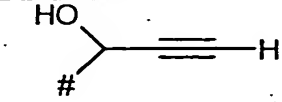
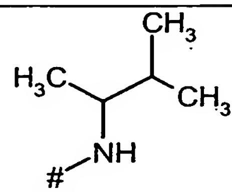
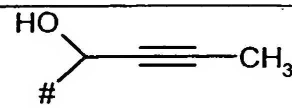
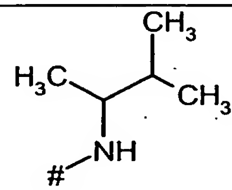
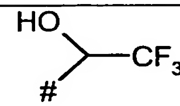
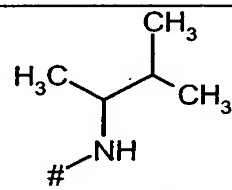
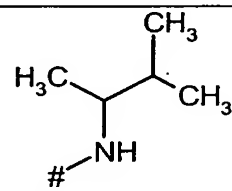
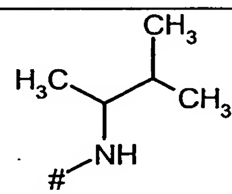
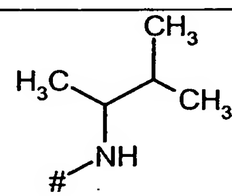
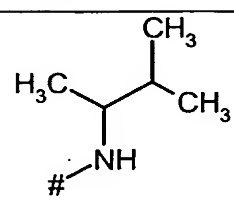
Ex. No.	N(R¹R²)	-C(R⁴R⁵(OR⁶))	logP
91		$-CH_2OH$	
92		$-CH_2-O-CH_3$	
93		allyloxymethyl	
94		$-CH_2-O-C_2H_5$	
95			
96			
97		1-hydroxyethyl	

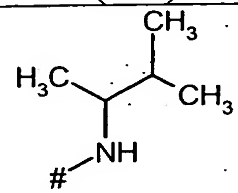
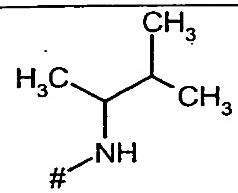
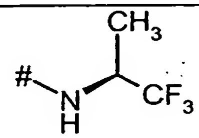
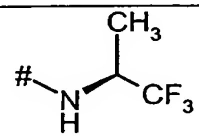
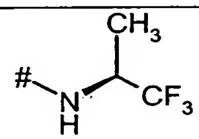
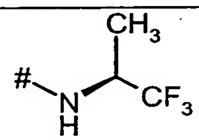
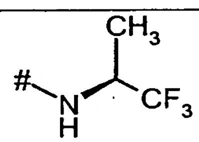
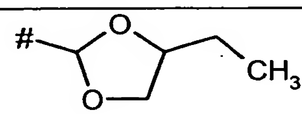
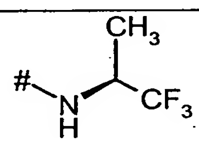
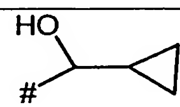
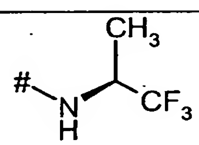
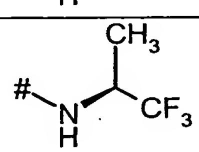
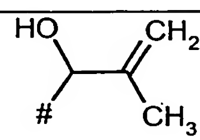
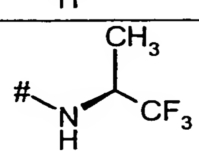
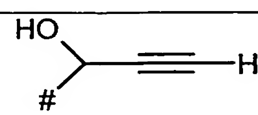
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
98			
99			
100			
101			
102		$-CH(OH)-CH_2Cl$	
103		$-CH(OH)-CH(CH_3)_2$	
104		$-CH(OH)-C(CH_3)_3$	
105		$-C(CH_3)(OH)-CH(CH_3)_2$	
106		$-CH(OCH_3)-CH(CH_3)_2$	
107		$-CH(CH_3)(OCH(CH_3)_2)$	
108		$-C(CH_3)(CF_3)-(OCH_3)$	
109		$-CH_2OH$	
110		$-CH_2-O-CH_3$	

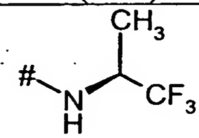
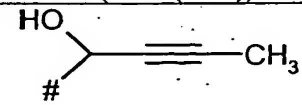
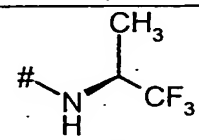
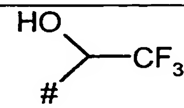
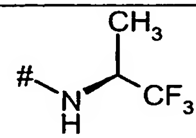
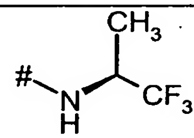
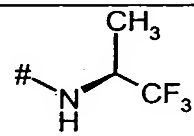
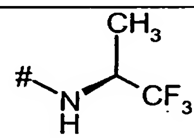
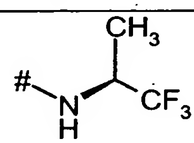
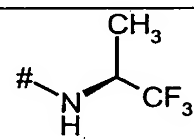
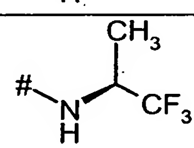
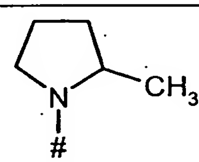
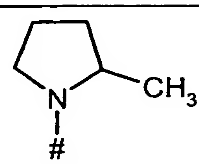
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
111		allyloxymethyl	
112		$-CH_2-O-C_2H_5$	
113			
114			
115		1-hydroxyethyl	
116			
117			
118			

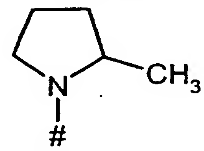
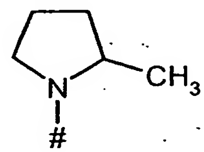
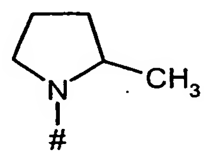
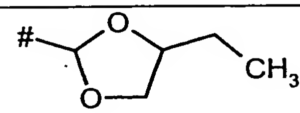
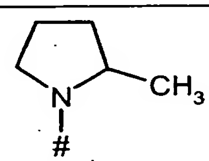
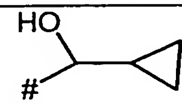
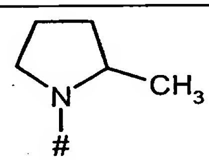
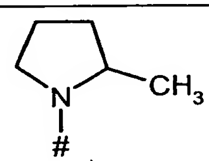
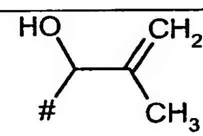
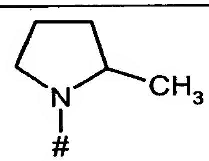
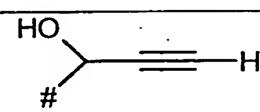
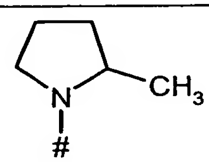
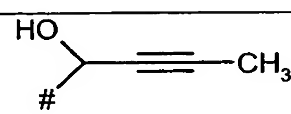
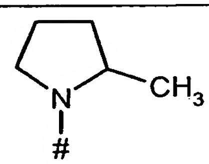
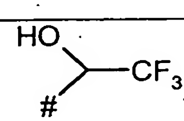
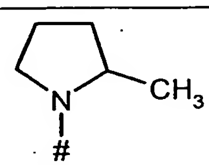
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
119			
120		$-CH(OH)-CH_2Cl$	
121		$-CH(OH)-CH(CH_3)_2$	
122		$-CH(OH)-C(CH_3)_3$	
123		$-C(CH_3)(OH)-CH(CH_3)_2$	
124		$-CH(OCH_3)-CH(CH_3)_2$	
125		$-CH(CH_3)(OCH(CH_3)_2)$	
126		$-C(CH_3)(CF_3)-(OCH_3)$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
127		$-CH_2OH$	
128		$-CH_2-O-CH_3$	
129		allyloxymethyl	
130		$-CH_2-O-C_2H_5$	
131			
132			
133		1-hydroxyethyl	
134			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
135			
136			
137			
138		$-CH(OH)-CH_2Cl$	
139		$-CH(OH)-CH(CH_3)_2$	
140		$-CH(OH)-C(CH_3)_3$	
141		$-C(CH_3)(OH)-CH(CH_3)_2$	
142		$-CH(OCH_3)-CH(CH_3)_2$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
143		$-CH(CH_3)(OCH(CH_3)_2)$	
144		$-C(CH_3)(CF_3)-(OCH_3)$	
145		$-CH_2OH$	
146		$-CH_2-O-CH_3$	
147		allyloxymethyl	
148		$-CH_2-O-C_2H_5$	
149			
150			
151		1-hydroxyethyl	
152			
153			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
154			
155			
156		$-CH(OH)-CH_2Cl$	
157		$-CH(OH)-CH(CH_3)_2$	
158		$-CH(OH)-C(CH_3)_3$	
159		$-C(CH_3)(OH)-CH(CH_3)_2$	
160		$-CH(OCH_3)-CH(CH_3)_2$	
161		$-CH(CH_3)(OCH(CH_3)_2)$	
162		$-C(CH_3)(CF_3)-(OCH_3)$	
163		$-CH_2OH$	
164		$-CH_2-O-CH_3$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
165		allyloxymethyl	
166		$-CH_2-O-C_2H_5$	
167			
168			
169		1-hydroxyethyl	
170			
171			
172			
173			
174		-CH(OH)-CH_2Cl	

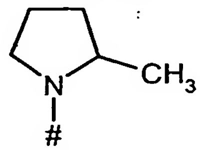
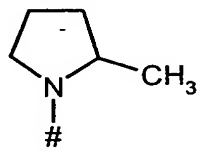
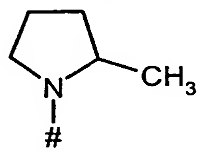
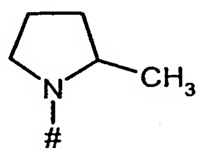
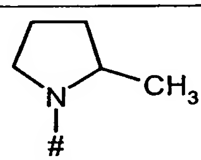
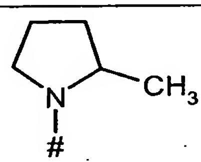
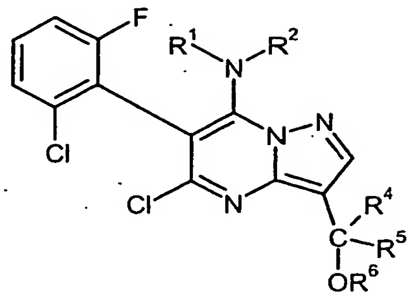
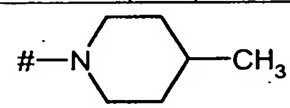
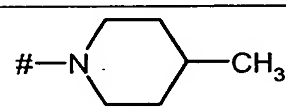
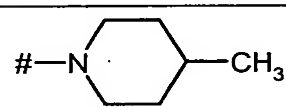
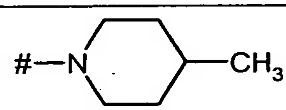
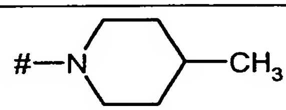
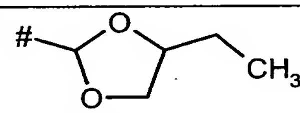
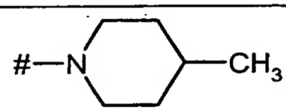
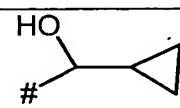
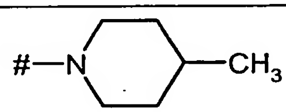
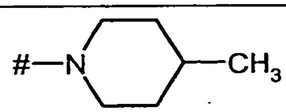
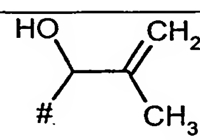
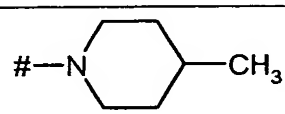
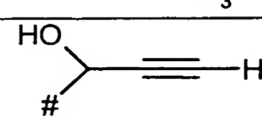
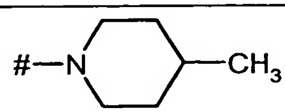
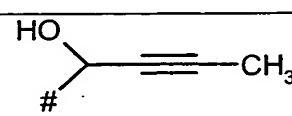
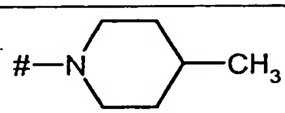
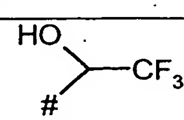
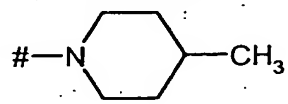
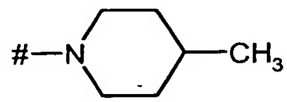
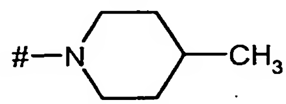
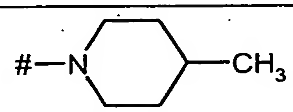
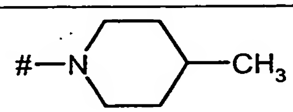
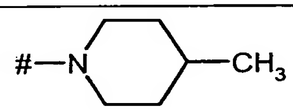
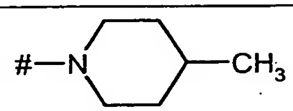
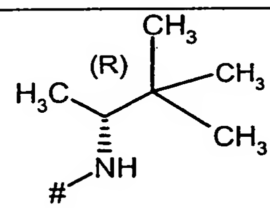
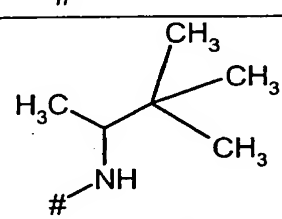
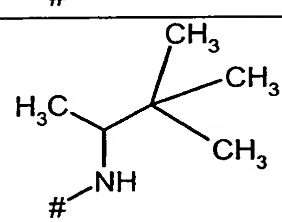
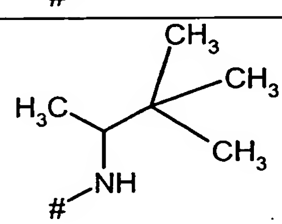
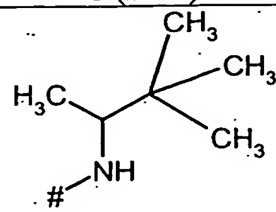
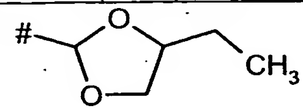
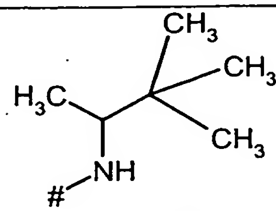
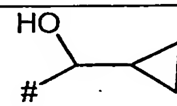
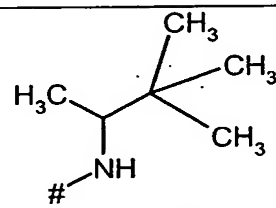
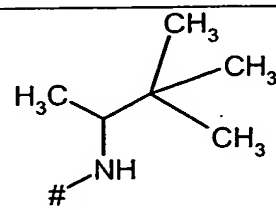
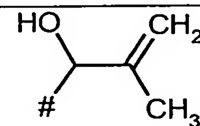
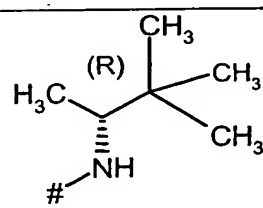
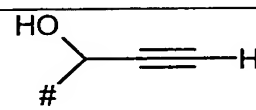
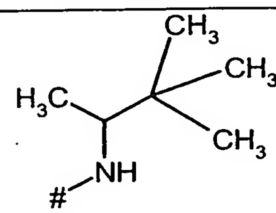
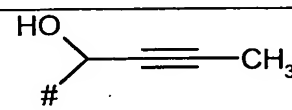
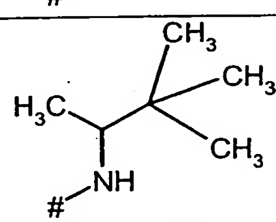
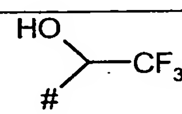
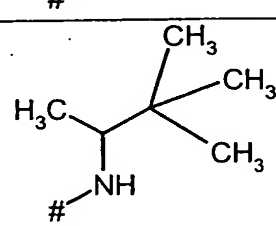
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
175		$-CH(OH)-CH(CH_3)_2$	
176		$-CH(OH)-C(CH_3)_3$	
177		$-C(CH_3)(OH)-CH(CH_3)_2$	
178		$-CH(OCH_3)-CH(CH_3)_2$	
179		$-CH(CH_3)(OCH(CH_3)_2)$	
180		$-C(CH_3)(CF_3)-(OCH_3)$	

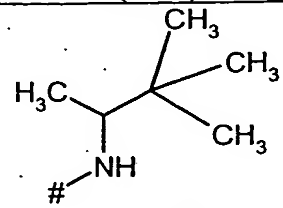
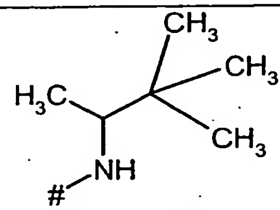
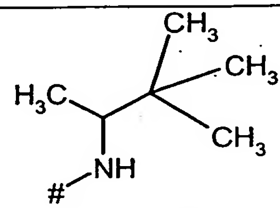
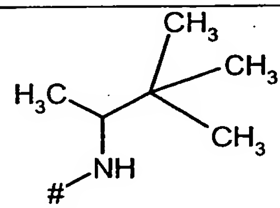
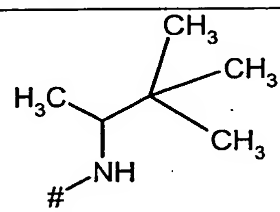
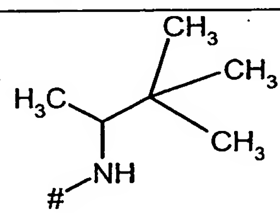
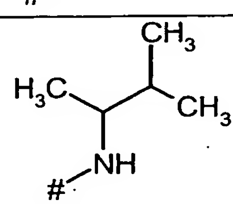
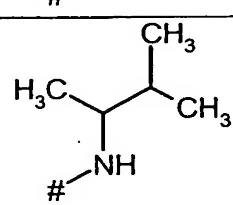
Table 3

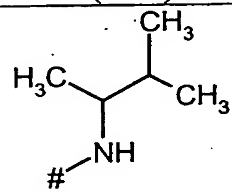
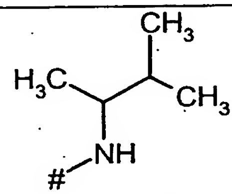
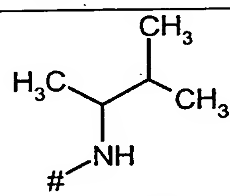
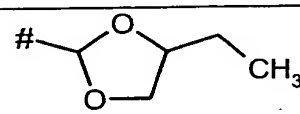
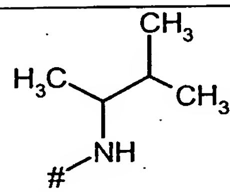
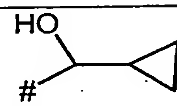
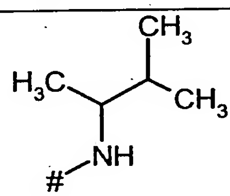
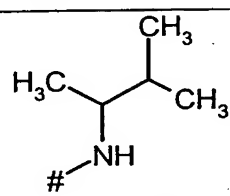
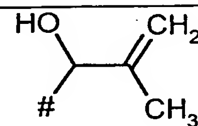
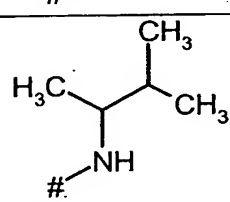
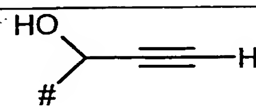
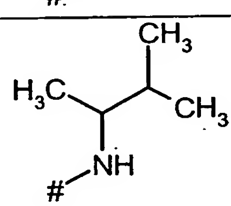
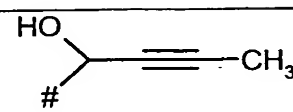


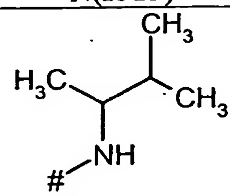
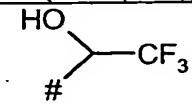
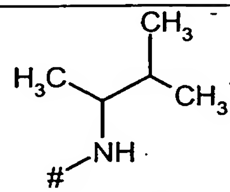
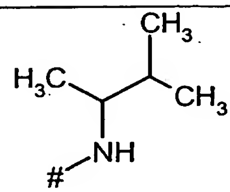
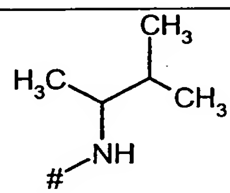
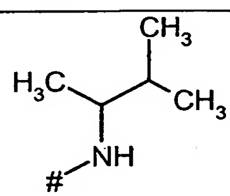
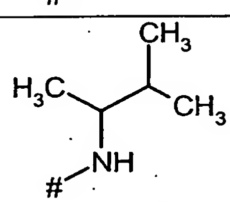
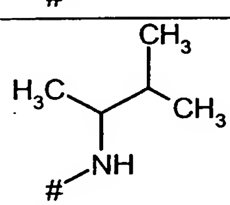
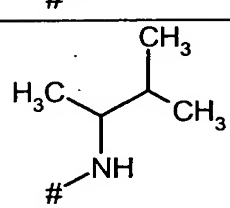
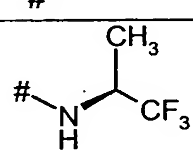
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
181		$-CH_2OH$	
182		$-CH_2-O-CH_3$	
183		allyloxymethyl	
184		$-CH_2-O-C_2H_5$	
185			
186			
187		1-hydroxyethyl	
188			
189			
190			
191			

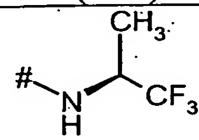
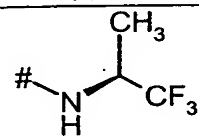
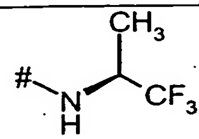
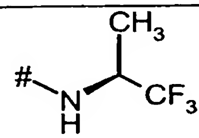
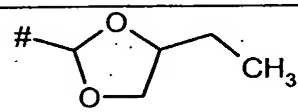
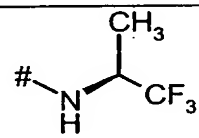
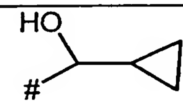
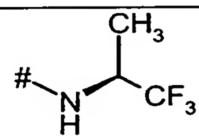
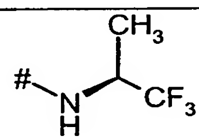
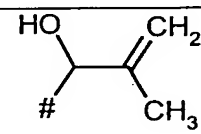
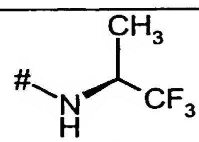
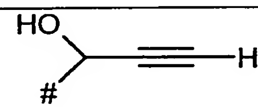
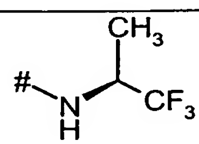
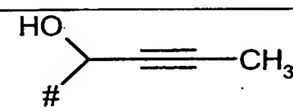
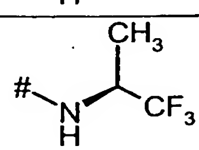
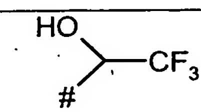
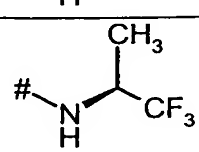
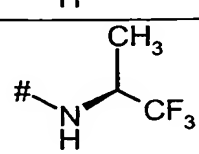
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
192		$-CH(OH)-CH_2Cl$	
193		$-CH(OH)-CH(CH_3)_2$	
194		$-CH(OH)-C(CH_3)_3$	
195		$-C(CH_3)(OH)-CH(CH_3)_2$	
196		$-CH(OCH_3)-CH(CH_3)_2$	
197		$-CH(CH_3)(OCH(CH_3)_2)$	
198		$-C(CH_3)(CF_3)-(OCH_3)$	
199		$-CH_2OH$	
200		$-CH_2-O-CH_3$	
201		allyloxymethyl	
202		$-CH_2-O-C_2H_5$	

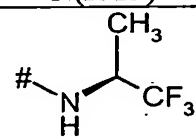
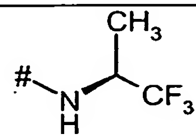
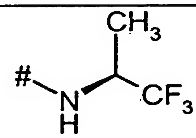
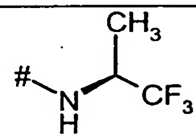
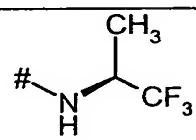
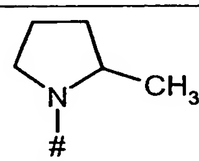
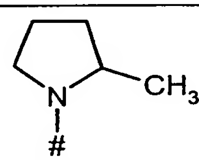
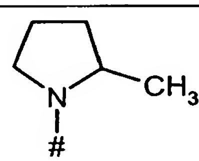
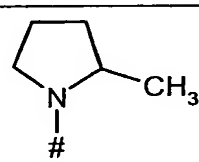
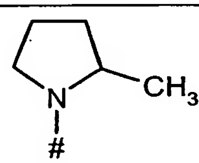
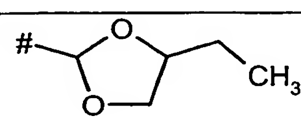
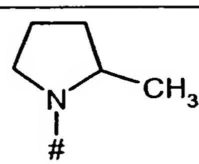
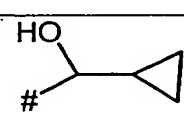
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
203			
204			
205		1-hydroxyethyl	
206			
207			
208			
209			
210		$-CH(OH)-CH_2Cl$	

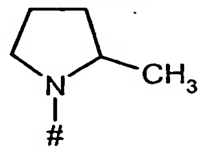
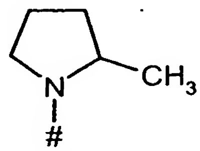
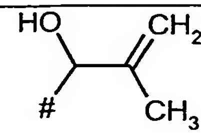
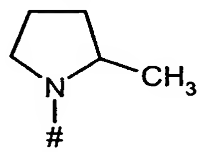
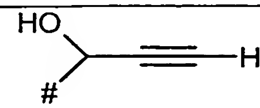
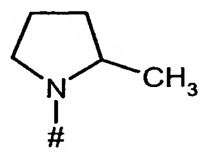
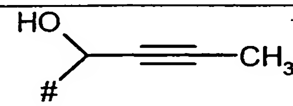
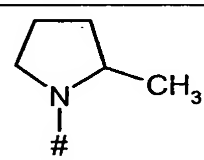
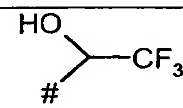
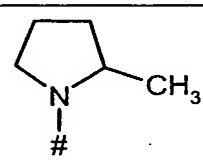
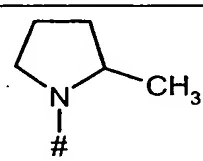
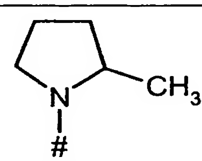
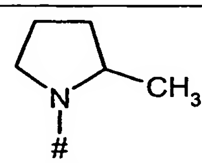
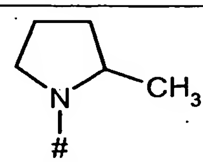
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
211		$-CH(OH)-CH(CH_3)_2$	
212		$-CH(OH)-C(CH_3)_3$	
213		$-C(CH_3)(OH)-CH(CH_3)_2$	
214		$-CH(OCH_3)-CH(CH_3)_2$	
215		$-CH(CH_3)(OCH(CH_3)_2)$	
216		$-C(CH_3)(CF_3)-(OCH_3)$	
217		$-CH_2OH$	
218		$-CH_2-O-CH_3$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
219		allyloxymethyl	
220		$-CH_2-O-C_2H_5$	
221			
222			
223		1-hydroxyethyl	
224			
225			
226			

Ex. No.	N(R¹R²)	-C(R⁴R⁵(OR⁶))	logP
227			
228		-CH(OH)-CH_2Cl	
229		-CH(OH)-CH$(CH_3)_2$	
230		-CH(OH)-C$(CH_3)_3$	
231		-C(CH_3)(OH)-CH$(CH_3)_2$	
232		-CH(OCH_3)-CH$(CH_3)_2$	
233		-CH(CH_3)(OCH$(CH_3)_2$)	
234		-C$(CH_3)(CF_3)$-(OCH_3)	
235		-CH_2OH	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
236		$-CH_2-O-CH_3$	
237		allyloxymethyl	
238		$-CH_2-O-C_2H_5$	
239			
240			
241		1-hydroxyethyl	
242			
243			
244			
245			
246		$-CH(OH)-CH_2Cl$	
247		$-CH(OH)-CH(CH_3)_2$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
248		$-CH(OH)-C(CH_3)_3$	
249		$-C(CH_3)(OH)-CH(CH_3)_2$	
250		$-CH(OCH_3)-CH(CH_3)_2$	
251		$-CH(CH_3)(OCH(CH_3)_2)$	
252		$-C(CH_3)(CF_3)-(OCH_3)$	
253		$-CH_2OH$	
254		$-CH_2-O-CH_3$	
255		allyloxymethyl	
256		$-CH_2-O-C_2H_5$	
257			
258			

Ex. No.	N(R[1]R[2])	-C(R[4]R[5](OR[6]))	logP
259		1-hydroxyethyl	
260			
261			
262			
263			
264		-CH(OH)-CH_2Cl	
265		-CH(OH)-$CH(CH_3)_2$	
266		-CH(OH)-$C(CH_3)_3$	
267		-$C(CH_3)$(OH)-$CH(CH_3)_2$	
268		-$CH(OCH_3)$-$CH(CH_3)_2$	

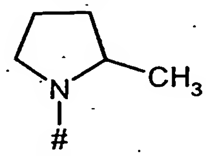
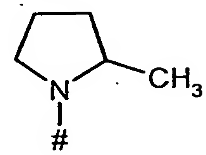
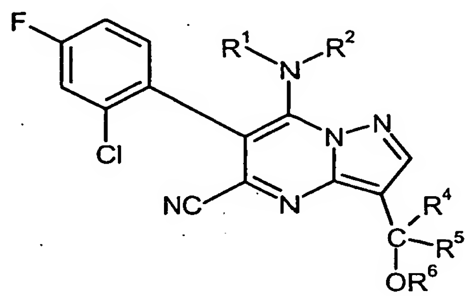
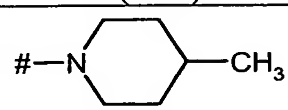
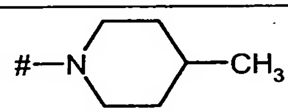
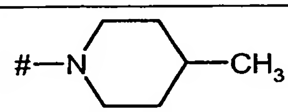
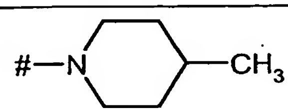
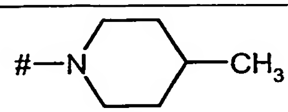
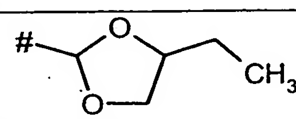
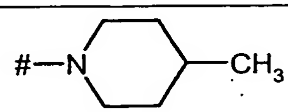
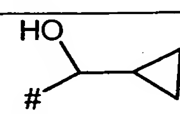
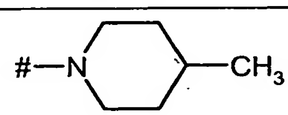
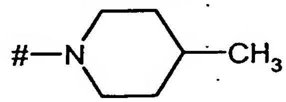
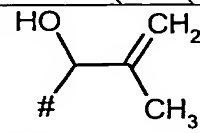
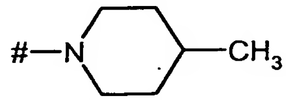
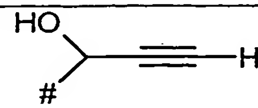
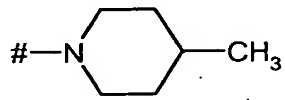
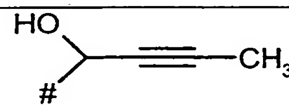
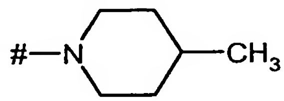
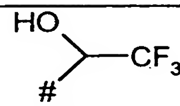
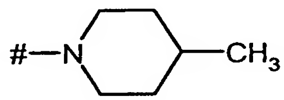
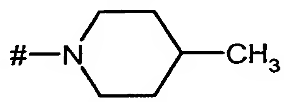
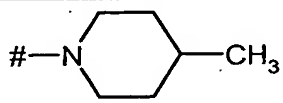
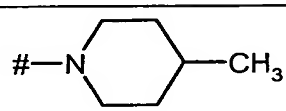
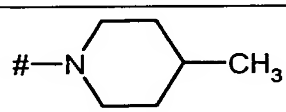
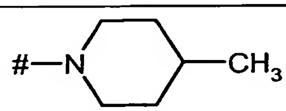
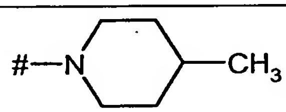
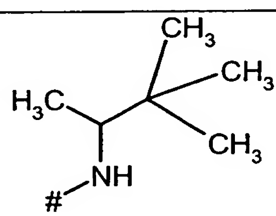
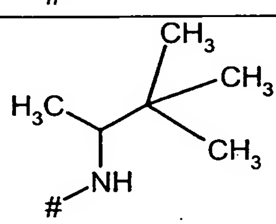
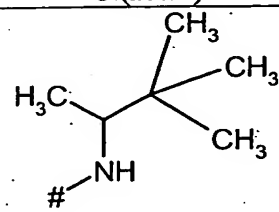
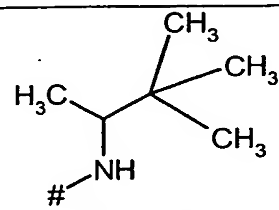
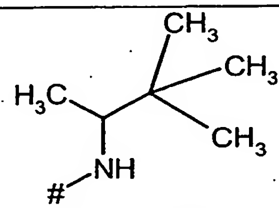
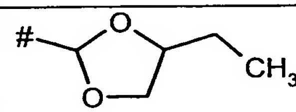
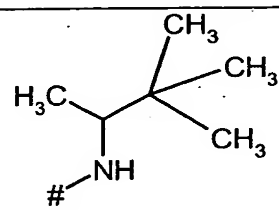
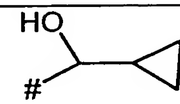
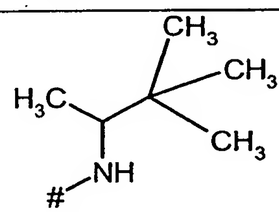
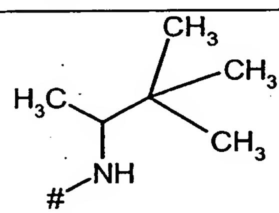
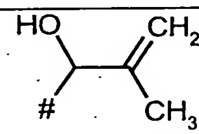
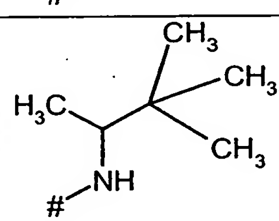
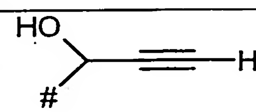
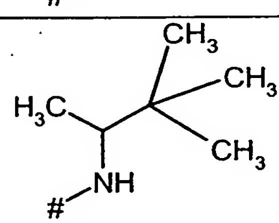
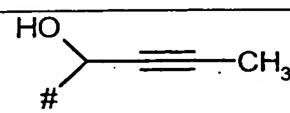
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
269		$-CH(CH_3)(OCH(CH_3)_2)$	
270		$-C(CH_3)(CF_3)-(OCH_3)$	

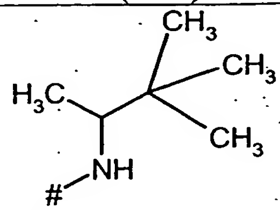
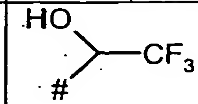
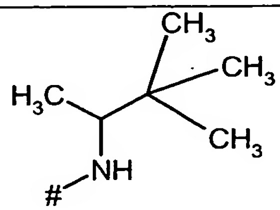
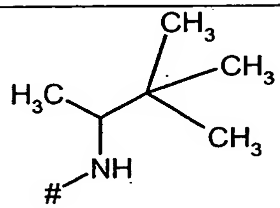
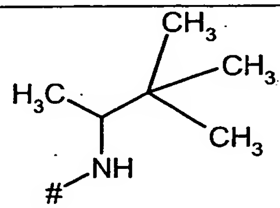
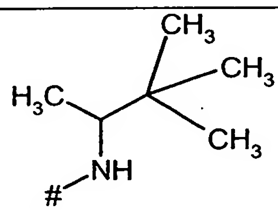
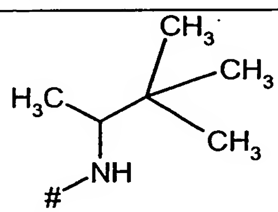
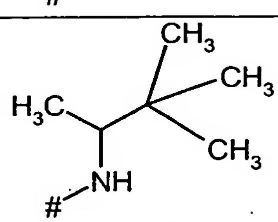
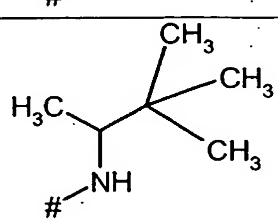
Table 4

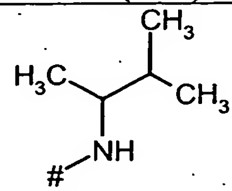
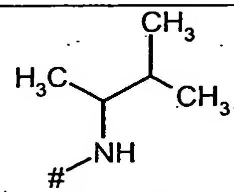
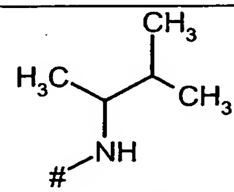
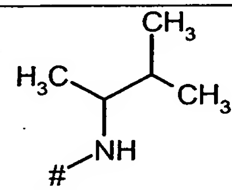
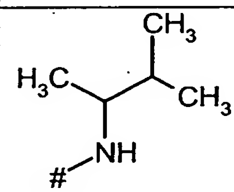
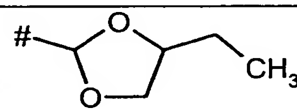
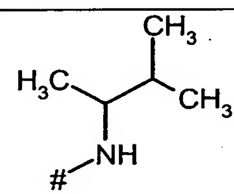
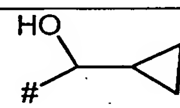
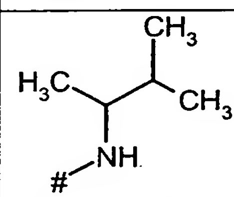
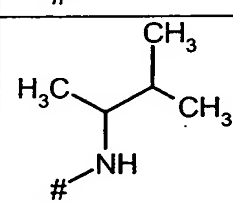
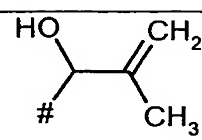


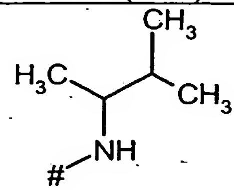
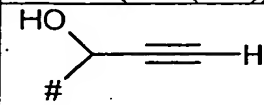
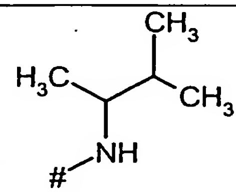
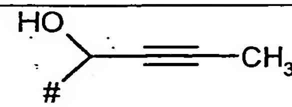
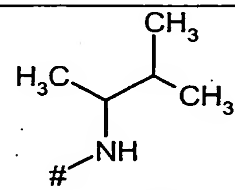
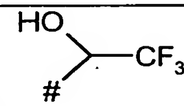
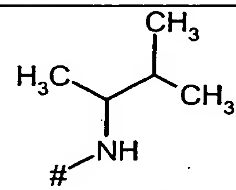
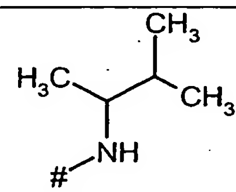
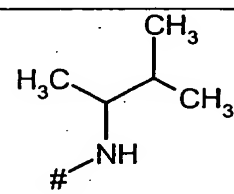
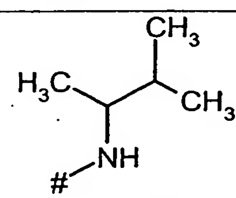
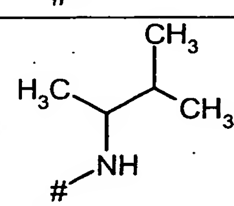
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
271		$-CH_2OH$	
272		$-CH_2-O-CH_3$	
273		allyloxymethyl	
274		$-CH_2-O-C_2H_5$	
275			
276			
277		1-hydroxyethyl	

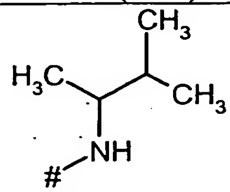
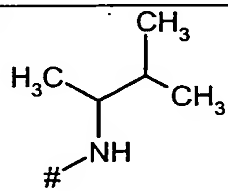
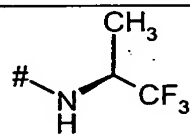
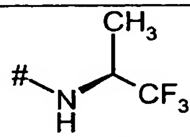
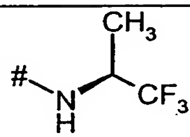
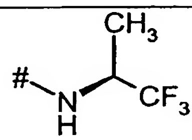
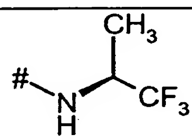
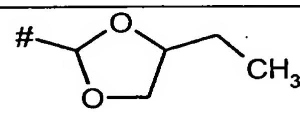
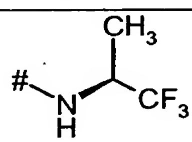
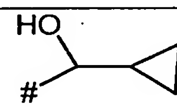
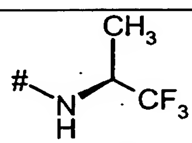
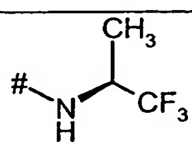
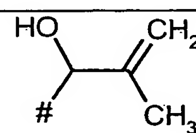
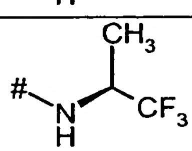
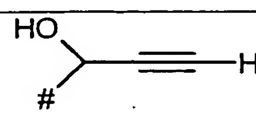
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
278			
279			
280			
281			
282		$-(CH(OH)-CH_2Cl$	
283		$-CH(OH)-CH(CH_3)_2$	
284		$-CH(OH)-C(CH_3)_3$	
285		$-C(CH_3)(OH)-CH(CH_3)_2$	
286		$-CH(OCH_3)-CH(CH_3)_2$	
287		$-CH(CH_3)(OCH(CH_3)_2)$	
288		$-C(CH_3)(CF_3)-(OCH_3)$	
289		$-CH_2OH$	
290		$-CH_2-O-CH_3$	

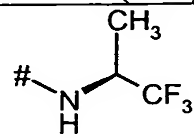
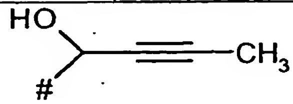
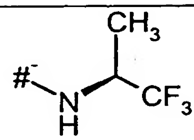
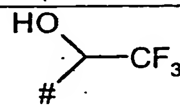
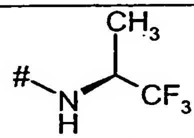
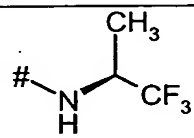
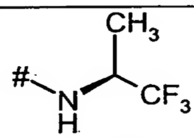
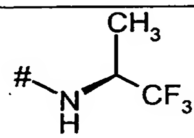
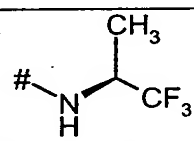
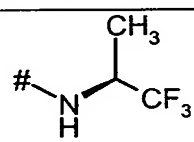
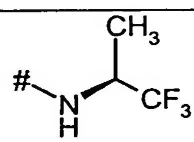
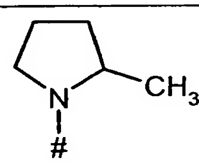
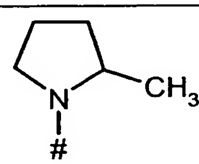
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
291		allyloxymethyl	
292		$-CH_2-O-C_2H_5$	
293			
294			
295		1-hydroxyethyl	
296			
297			
298			

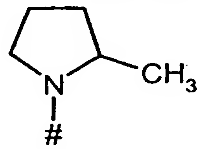
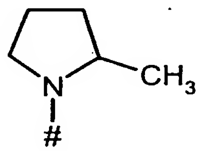
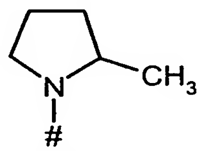
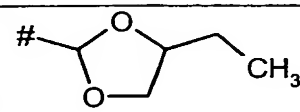
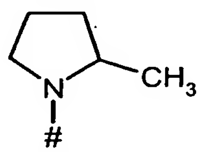
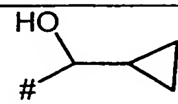
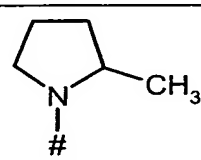
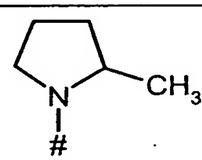
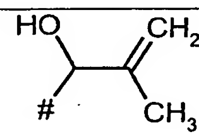
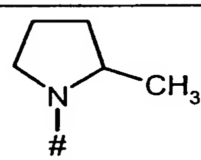
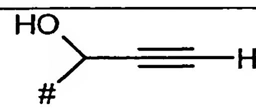
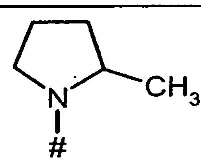
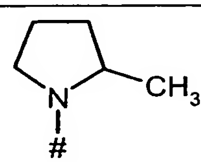
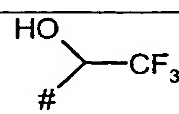
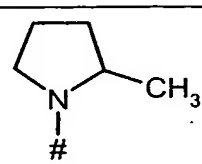
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
299			
300		$-(CH(OH)-CH_2Cl$	
301		$-CH(OH)-CH(CH_3)_2$	
302		$-CH(OH)-C(CH_3)_3$	
303		$-C(CH_3)(OH)-CH(CH_3)_2$	
304		$-CH(OCH_3)-CH(CH_3)_2$	
305		$-CH(CH_3)(OCH(CH_3)_2)$	
306		$-C(CH_3)(CF_3)-(OCH_3)$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
307		$-CH_2OH$	
308		$-CH_2-O-CH_3$	
309		allyloxymethyl	
310		$-CH_2-O-C_2H_5$	
311			
312			
313		1-hydroxyethyl	
314			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
315			
316			
317			
318		-(CH(OH)-CH_2Cl	
319		-CH(OH)-CH(CH_3)$_2$	
320		-CH(OH)-C(CH_3)$_3$	
321		-C(CH_3)(OH)-CH(CH_3)$_2$	
322		-CH(OCH_3)-CH(CH_3)$_2$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
323		$-CH(CH_3)(OCH(CH_3)_2)$	
324		$-C(CH_3)(CF_3)-(OCH_3)$	
325		$-CH_2OH$	
326		$-CH_2-O-CH_3$	
327		allyloxymethyl	
328		$-CH_2-O-C_2H_5$	
329			
330			
331		1-hydroxyethyl	
332			
333			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
334			
335			
336		$-(CH(OH)-CH_2Cl$	
337		$-CH(OH)-CH(CH_3)_2$	
338		$-CH(OH)-C(CH_3)_3$	
339		$-C(CH_3)(OH)-CH(CH_3)_2$	
340		$-CH(OCH_3)-CH(CH_3)_2$	
341		$-CH(CH_3)(OCH(CH_3)_2)$	
342		$-C(CH_3)(CF_3)-(OCH_3)$	
343		$-CH_2OH$	
344		$-CH_2-O-CH_3$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
345		allyloxymethyl	
346		$-CH_2-O-C_2H_5$	
347			
348			
349		1-hydroxyethyl	
350			
351			
352			
353			
354		$-(CH(OH)-CH_2Cl$	

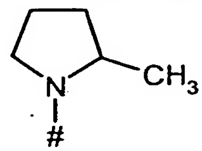
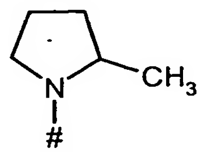
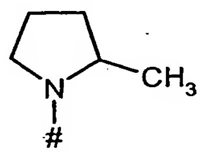
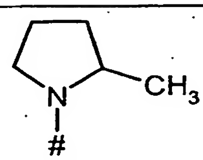
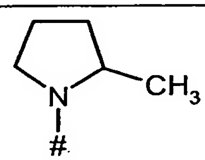
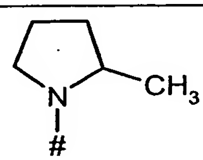
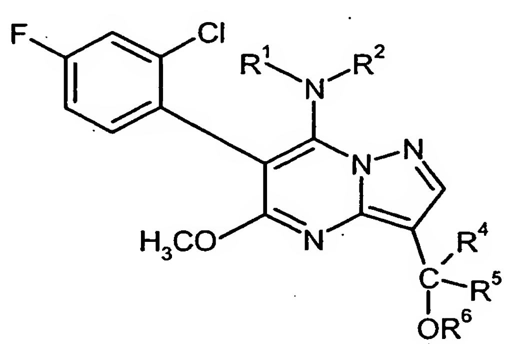
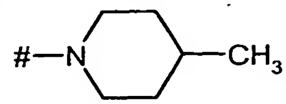
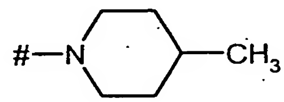
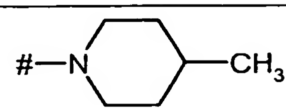
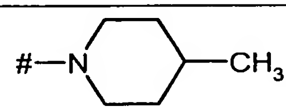
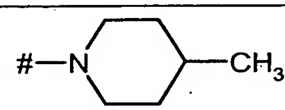
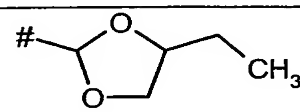
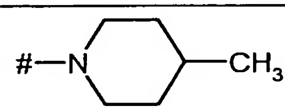
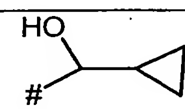
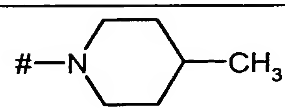
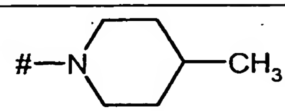
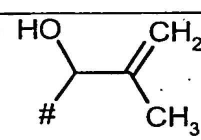
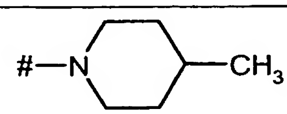
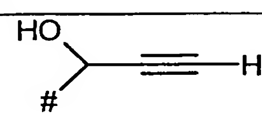
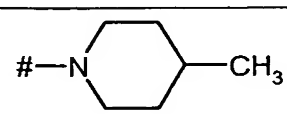
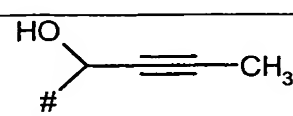
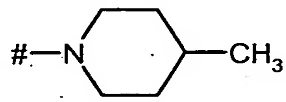
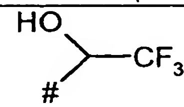
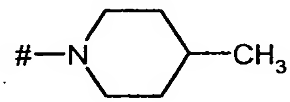
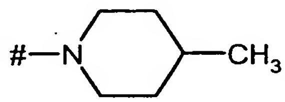
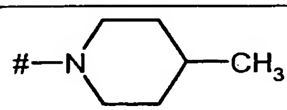
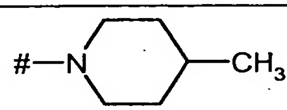
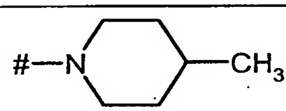
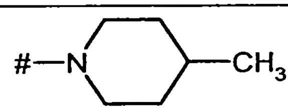
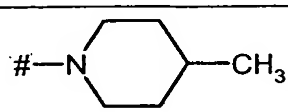
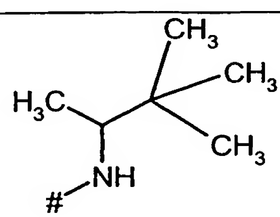
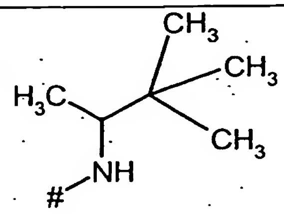
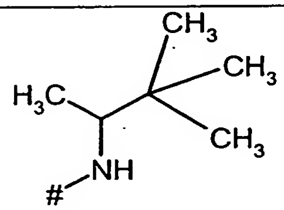
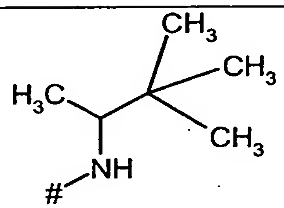
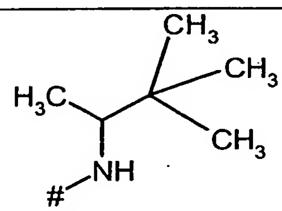
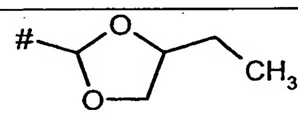
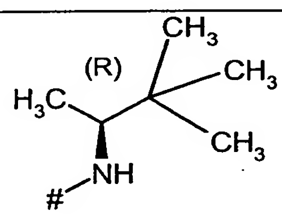
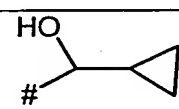
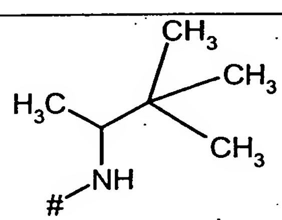
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
355		$-CH(OH)-CH(CH_3)_2$	
356		$-CH(OH)-C(CH_3)_3$	
357		$-C(CH_3)(OH)-CH(CH_3)_2$	
358		$-CH(OCH_3)-CH(CH_3)_2$	
359		$-CH(CH_3)(OCH(CH_3)_2)$	
360		$-C(CH_3)(CF_3)-(OCH_3)$	

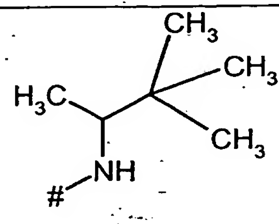
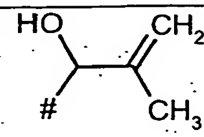
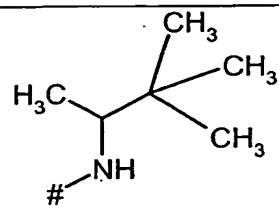
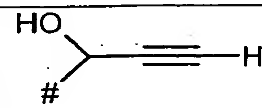
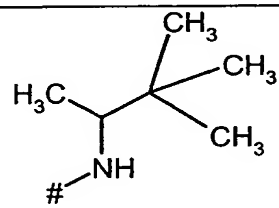
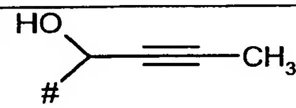
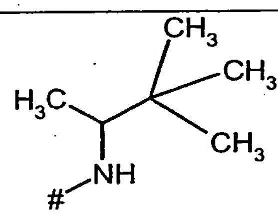
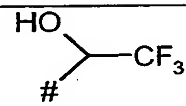
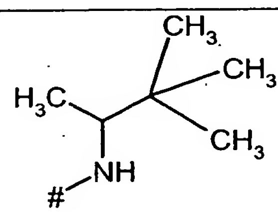
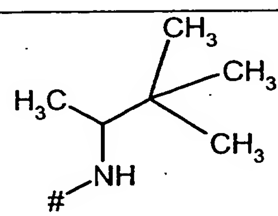
Table 5

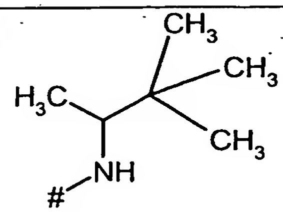
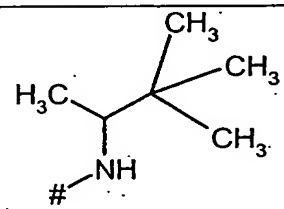
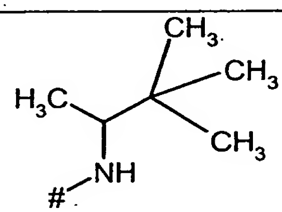
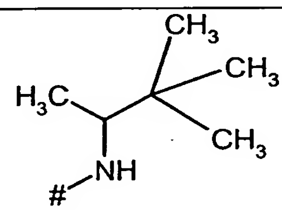
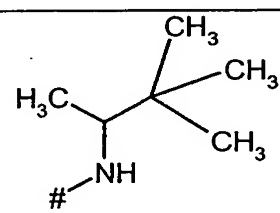
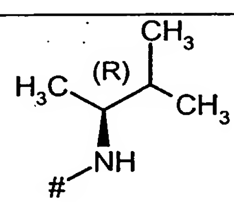


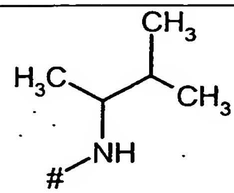
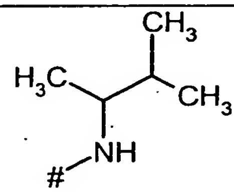
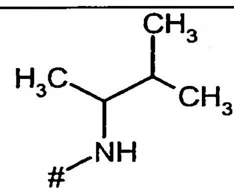
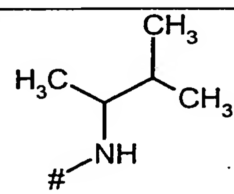
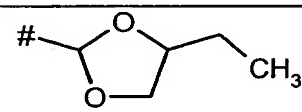
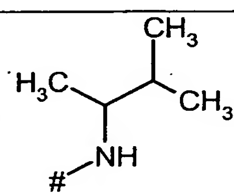
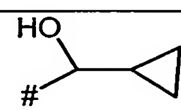
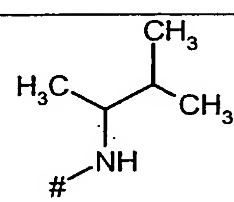
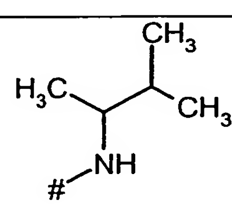
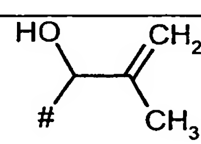
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
361		$-CH_2OH$	
362		$-CH_2-O-CH_3$	
363		allyloxymethyl	
364		$-CH_2-O-C_2H_5$	
365			
366			
367		1-hydroxyethyl	
368			
369			
370			

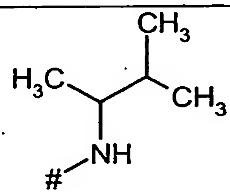
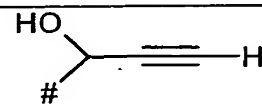
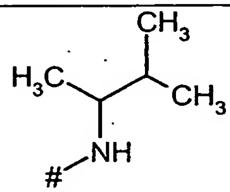
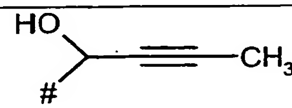
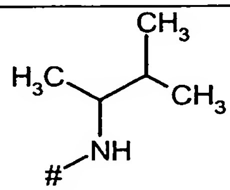
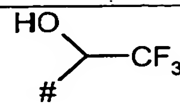
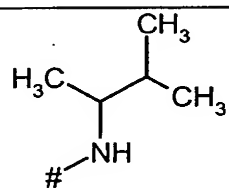
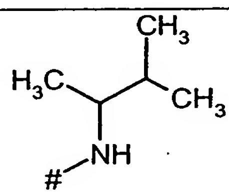
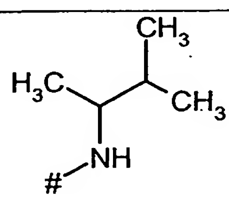
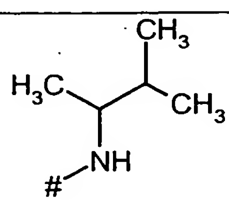
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
371			
372		$-(CH(OH)-CH_2Cl$	
373		$-CH(OH)-CH(CH_3)_2$	
374		$-CH(OH)-C(CH_3)_3$	
375		$-C(CH_3)(OH)-CH(CH_3)_2$	
376		$-CH(OCH_3)-CH(CH_3)_2$	
377		$-CH(CH_3)(OCH(CH_3)_2)$	
378		$-C(CH_3)(CF_3)-(OCH_3)$	
379		$-CH_2OH$	4.14

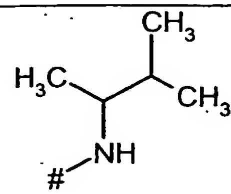
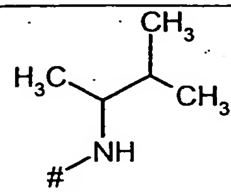
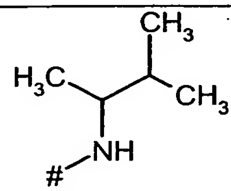
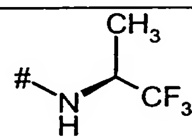
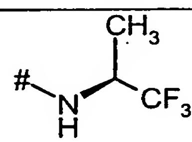
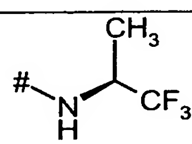
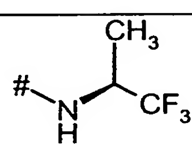
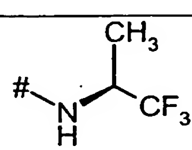
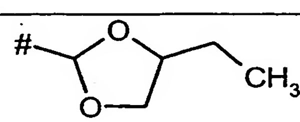
Ex. No.	N(R¹R²)	-C(R⁴R⁵(OR⁶))	logP
380		$-CH_2-O-CH_3$	
381		allyloxymethyl	
382		$-CH_2-O-C_2H_5$	
383			
384			
385		1-hydroxyethyl	

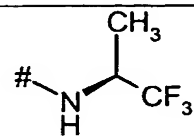
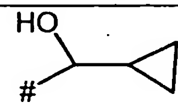
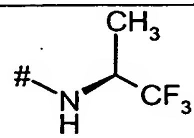
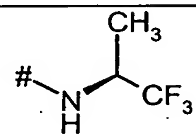
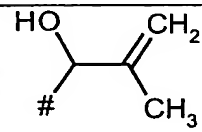
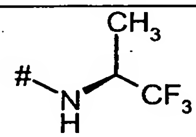
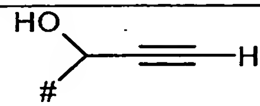
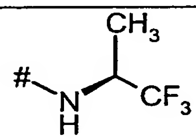
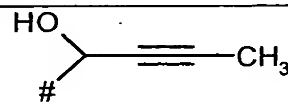
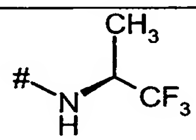
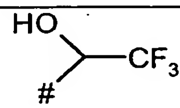
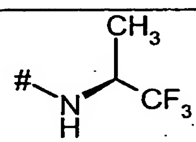
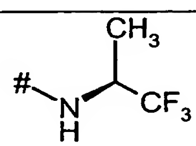
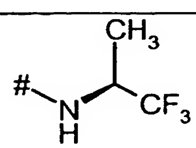
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
386			
387			
388			
389			
390		-(CH(OH)-CH_2Cl	
391		-CH(OH)-$CH(CH_3)_2$	

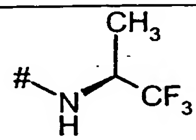
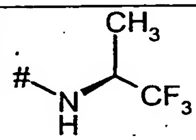
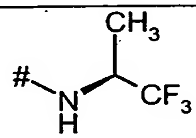
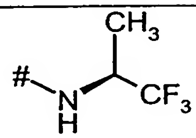
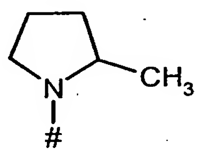
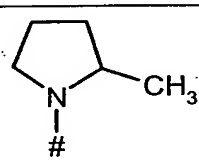
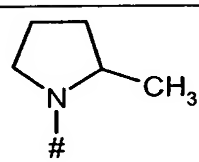
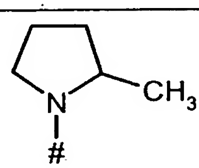
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
392		$-CH(OH)-C(CH_3)_3$	
393		$-C(CH_3)(OH)-CH(CH_3)_2$	
394		$-CH(OCH_3)-CH(CH_3)_2$	
395		$-CH(CH_3)(OCH(CH_3)_2)$	
396		$-C(CH_3)(CF_3)-(OCH_3)$	
397		$-CH_2OH$	

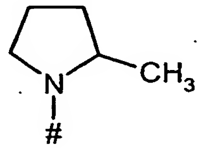
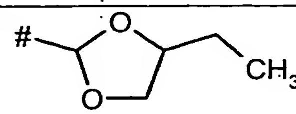
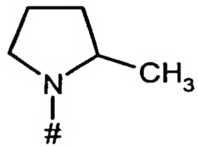
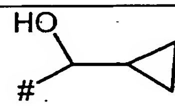
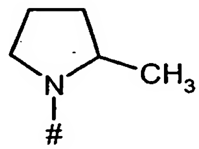
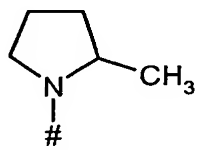
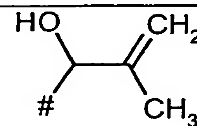
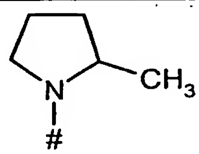
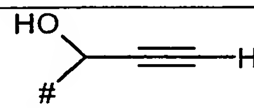
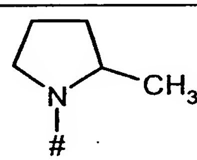
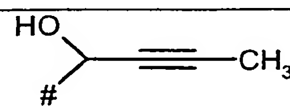
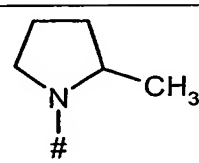
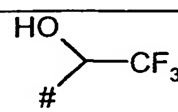
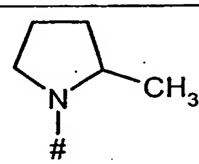
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
398		$-CH_2-O-CH_3$	
399		allyloxymethyl	
400		$-CH_2-O-C_2H_5$	
401			
402			
403		1-hydroxyethyl	
404			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
405			
406			
407			
408		$-(CH(OH)-CH_2Cl$	
409		$-CH(OH)-CH(CH_3)_2$	
410		$-CH(OH)-C(CH_3)_3$	
411		$-C(CH_3)(OH)-CH(CH_3)_2$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
412		$-CH(OCH_3)-CH(CH_3)_2$	
413		$-CH(CH_3)(OCH(CH_3)_2)$	
414		$-C(CH_3)(CF_3)-(OCH_3)$	
415		$-CH_2OH$	
416		$-CH_2-O-CH_3$	
417		allyloxymethyl	
418		$-CH_2-O-C_2H_5$	
419			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
420			
421		1-hydroxyethyl	
422			
423			
424			
425			
426		$-(CH(OH)-CH_2Cl$	
427		$-CH(OH)-CH(CH_3)_2$	
428		$-CH(OH)-C(CH_3)_3$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
429		$-C(CH_3)(OH)-CH(CH_3)_2$	
430		$-CH(OCH_3)-CH(CH_3)_2$	
431		$-CH(CH_3)(OCH(CH_3)_2)$	
432		$-C(CH_3)(CF_3)-(OCH_3)$	
433		$-CH_2OH$	
434		$-CH_2-O-CH_3$	
435		allyloxymethyl	
436		$-CH_2-O-C_2H_5$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
437			
438			
439		1-hydroxyethyl	
440			
441			
442			
443			
444		$-(CH(OH)-CH_2Cl$	

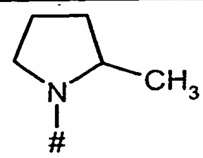
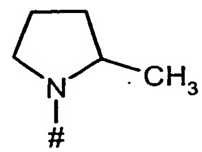
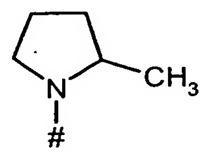
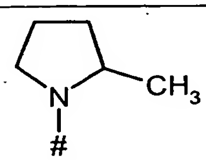
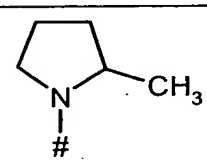
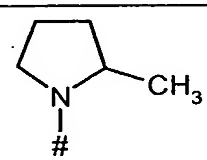
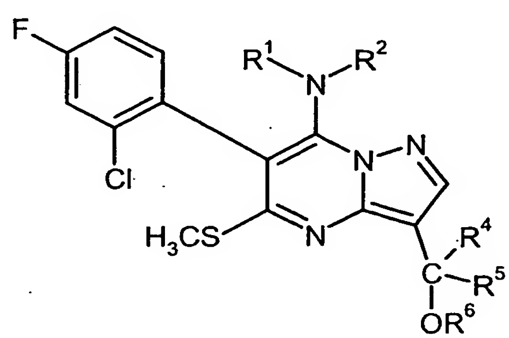
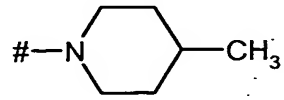
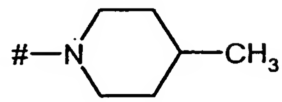
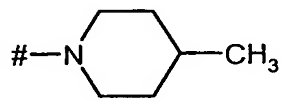
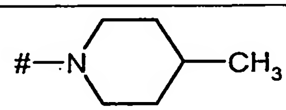
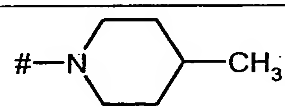
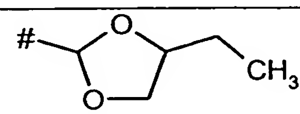
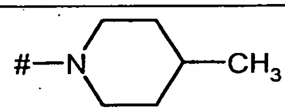
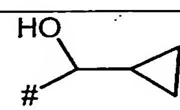
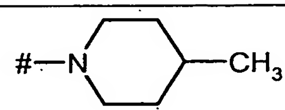
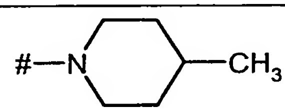
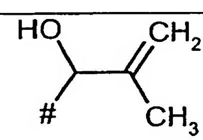
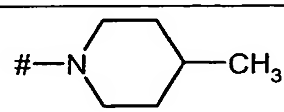
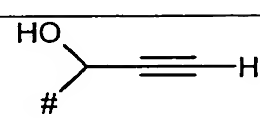
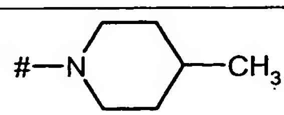
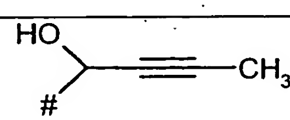
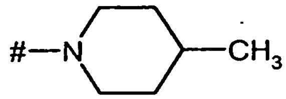
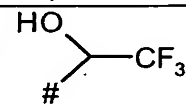
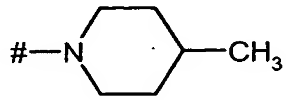
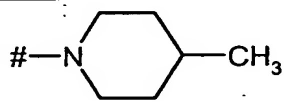
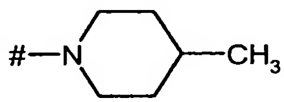
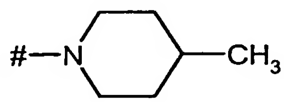
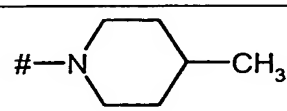
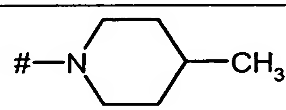
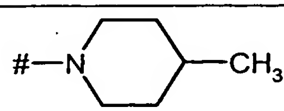
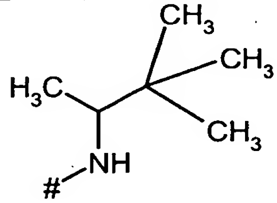
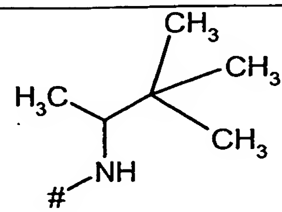
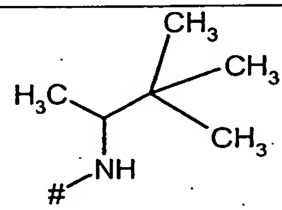
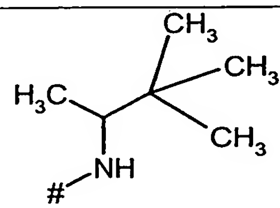
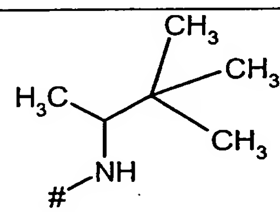
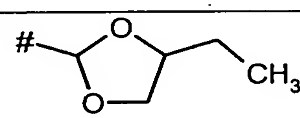
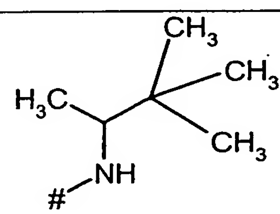
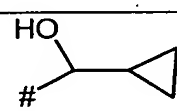
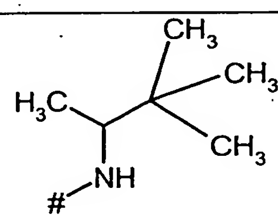
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
445		$-CH(OH)-CH(CH_3)_2$	
446		$-CH(OH)-C(CH_3)_3$	
447		$-C(CH_3)(OH)-CH(CH_3)_2$	
448		$-CH(OCH_3)-CH(CH_3)_2$	
449		$-CH(CH_3)(OCH(CH_3)_2)$	
450		$-C(CH_3)(CF_3)-(OCH_3)$	

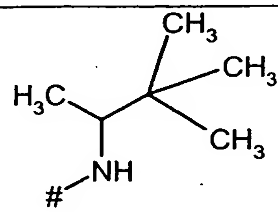
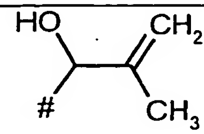
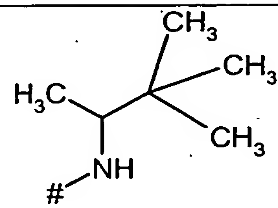
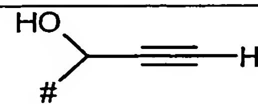
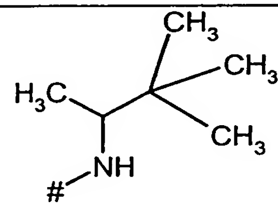
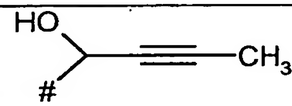
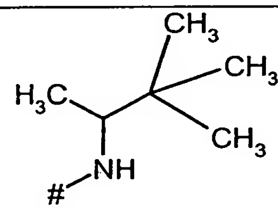
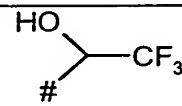
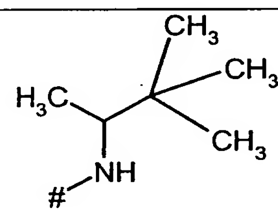
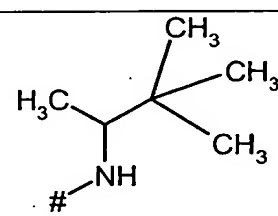
Table 6

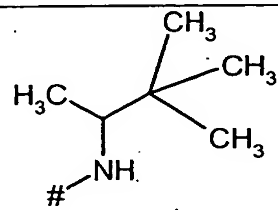
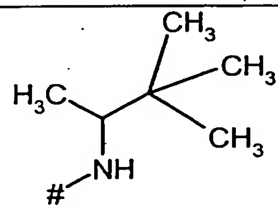
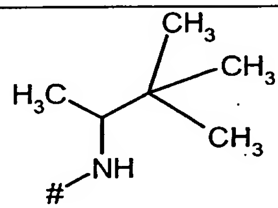
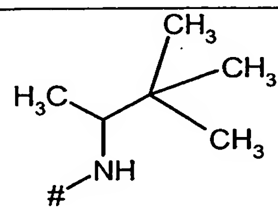
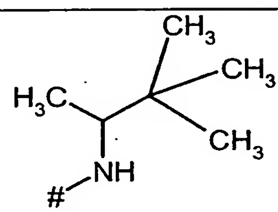
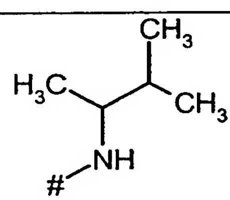


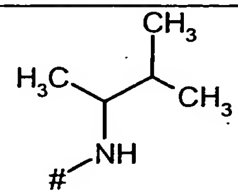
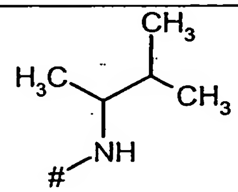
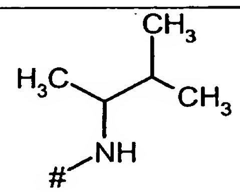
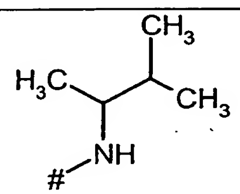
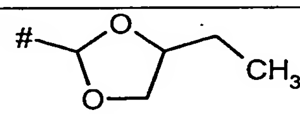
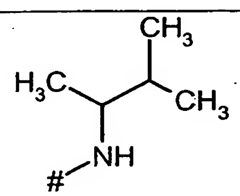
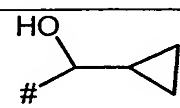
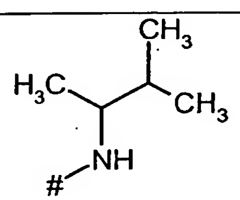
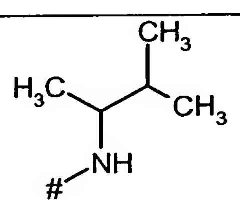
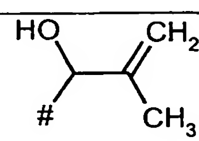
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
451		$-CH_2OH$	
452		$-CH_2-O-CH_3$	
453		allyloxymethyl	
454		$-CH_2-O-C_2H_5$	
455			
456			
457		1-hydroxyethyl	
458			
459			
460			

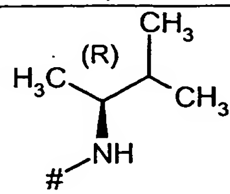
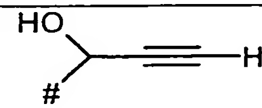
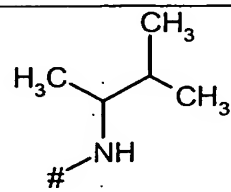
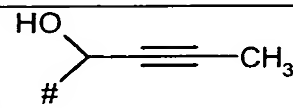
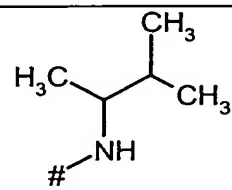
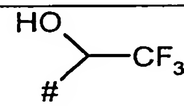
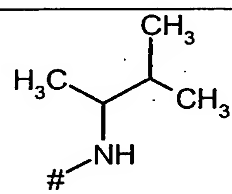
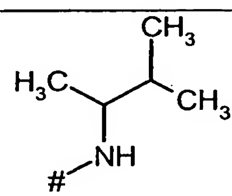
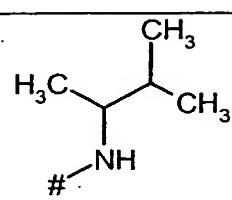
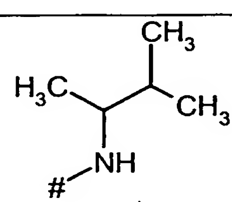
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
461			
462		$-(CH(OH)-CH_2Cl$	
463		$-CH(OH)-CH(CH_3)_2$	
464		$-CH(OH)-C(CH_3)_3$	
465		$-C(CH_3)(OH)-CH(CH_3)_2$	
466		$-CH(OCH_3)-CH(CH_3)_2$	
467		$-CH(CH_3)(OCH(CH_3)_2)$	
468		$-C(CH_3)(CF_3)-(OCH_3)$	
469		$-CH_2OH$	4.38

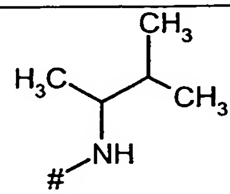
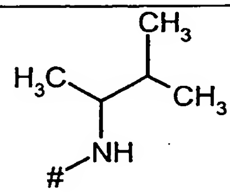
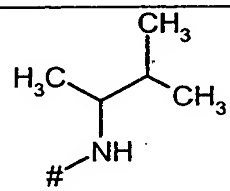
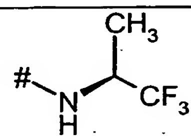
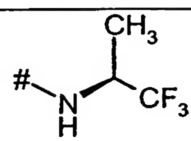
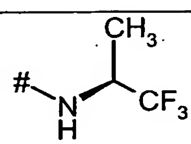
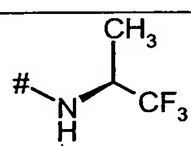
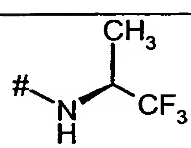
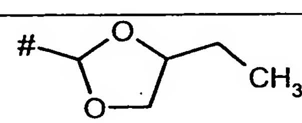
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
470		$-CH_2-O-CH_3$	
471		allyloxymethyl	
472		$-CH_2-O-C_2H_5$	
473			
474			
475		1-hydroxyethyl	

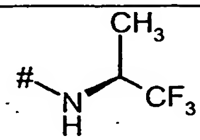
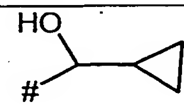
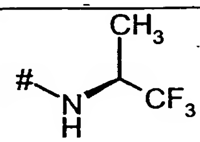
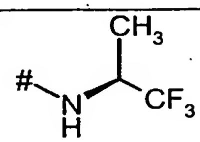
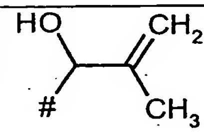
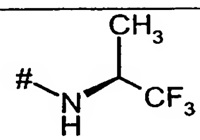
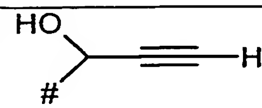
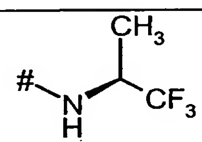
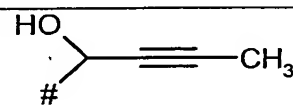
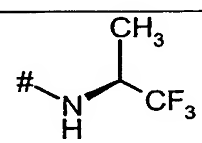
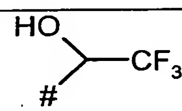
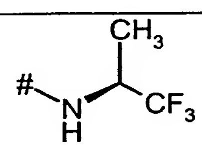
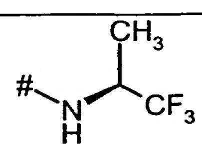
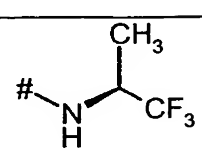
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
476			
477			
478			
479			
480		-(CH(OH)-CH_2Cl	
481		-CH(OH)-CH$(CH_3)_2$	

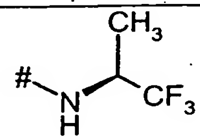
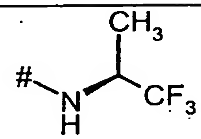
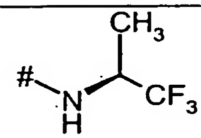
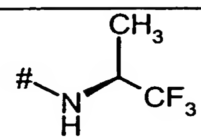
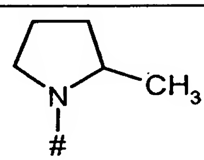
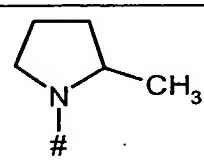
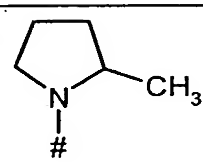
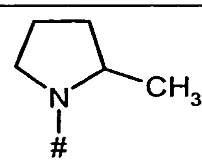
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
482		$-CH(OH)-C(CH_3)_3$	
483		$-C(CH_3)(OH)-CH(CH_3)_2$	
484		$-CH(OCH_3)-CH(CH_3)_2$	
485		$-CH(CH_3)(OCH(CH_3)_2)$	
486		$-C(CH_3)(CF_3)-(OCH_3)$	
487		$-CH_2OH$	

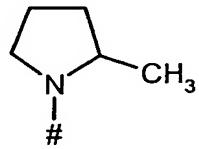
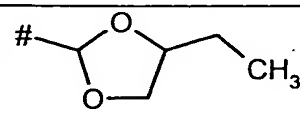
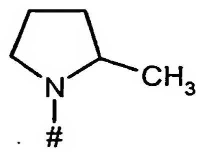
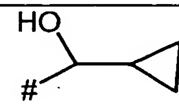
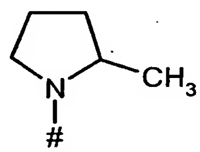
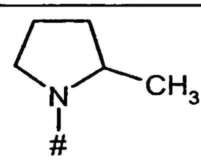
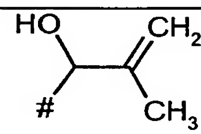
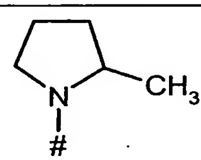
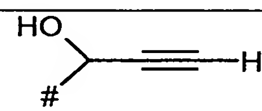
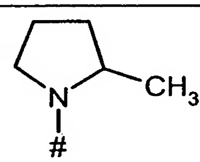
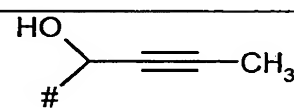
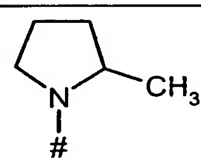
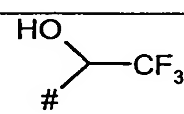
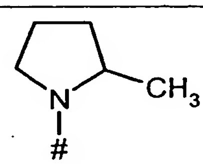
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
488		$-CH_2-O-CH_3$	
489		allyloxymethyl	
490		$-CH_2-O-C_2H_5$	
491			
492			
493		1-hydroxyethyl	
494			

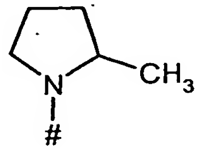
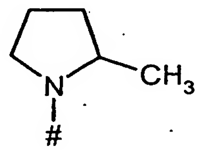
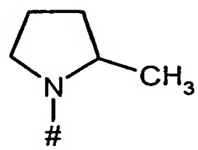
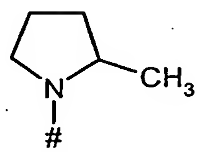
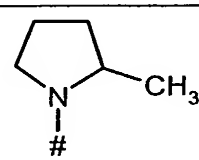
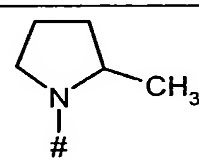
Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
495			
496			
497			
498		$-(CH(OH)-CH_2Cl$	
499		$-CH(OH)-CH(CH_3)_2$	
500		$-CH(OH)-C(CH_3)_3$	
501		$-C(CH_3)(OH)-CH(CH_3)_2$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
502		$-CH(OCH_3)-CH(CH_3)_2$	
503		$-CH(CH_3)(OCH(CH_3)_2)$	
504		$-C(CH_3)(CF_3)-(OCH_3)$	
505		$-CH_2OH$	
506		$-CH_2-O-CH_3$	
507		allyloxymethyl	
508		$-CH_2-O-C_2H_5$	
509			

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
510			
511		1-hydroxyethyl	
512			
513			
514			
515			
516		$-(CH(OH)-CH_2Cl$	
517		$-CH(OH)-CH(CH_3)_2$	
518		$-CH(OH)-C(CH_3)_3$	

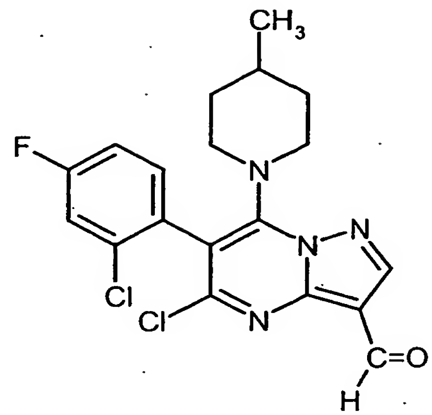
Ex. No.	N(R¹R²)	-C(R⁴R⁵(OR⁶))	logP
519		$-C(CH_3)(OH)-CH(CH_3)_2$	
520		$-CH(OCH_3)-CH(CH_3)_2$	
521		$-CH(CH_3)(OCH(CH_3)_2)$	
522		$-C(CH_3)(CF_3)-(OCH_3)$	
523		$-CH_2OH$	
524		$-CH_2-O-CH_3$	
525		allyloxymethyl	
526		$-CH_2-O-C_2H_5$	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
527			
528			
529		1-hydroxyethyl	
530			
531			
532			
533			
534		-(CH(OH)-CH_2Cl	

Ex. No.	$N(R^1R^2)$	$-C(R^4R^5(OR^6))$	logP
535		$-CH(OH)-CH(CH_3)_2$	
536		$-CH(OH)-C(CH_3)_3$	
537		$-C(CH_3)(OH)-CH(CH_3)_2$	
538		$-CH(OCH_3)-CH(CH_3)_2$	
539		$-CH(CH_3)(OCH(CH_3)_2)$	
540		$-C(CH_3)(CF_3)-(OCH_3)$	

Preparation of starting materials

Example 541



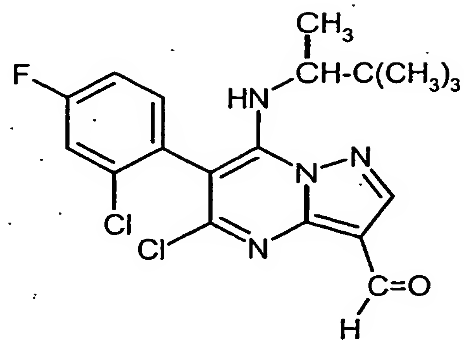
Process (e):

At 0°C, 41 mmol of N,N-dimethylformamide are added dropwise with stirring to a mixture of 37.2 mmol of 5,7-dihydroxy-6-(2-chloro-4-fluorophenyl)pyrazolo[1,5-a]pyrimidine and 372 mmol phosphorus oxychloride. After the addition has ended, the mixture is initially stirred at room temperature for 12 hours and then heated at reflux temperature for 6 hours. During this time, 37.2 mmol of phosphorus pentachloride are added a little at a time. After subsequent cooling to room temperature, the reaction mixture is added to ice-water. The resulting mixture is extracted three time with ethyl acetate. The combined organic phases are dried over sodium sulfate and then made up to twice the original volume by addition of cyclohexane. The solution is filtered through silica gel and then concentrated under reduced pressure. This gives 3-formyl-5,7-dichloro-6-(2-chloro-4-fluorophenyl)pyrazolo[1,5-a]pyrimidine in the form of a crude product which is used without additional purification for further synthesis.

At room temperature, 2.4 mmol of 4-methylpiperidine and 2.4 mmol of triethylamine are added with stirring to a mixture of 2.2 mmol of 3-formyl-5,7-dichloro-6-(2-chloro-4-fluorophenyl)pyrazolo[1,5-a]pyrimidine and 50 ml of dichloromethane. The mixture is stirred at room temperature for 15 hours and then poured into water. The organic phase is removed, and the aqueous phase is extracted three times with ethyl acetate. The combined organic phases are dried over sodium sulfate and then concentrated under reduced pressure. The residue that remains is chromatographed on silica gel using cyclohexane:ethyl acetate = 9:1. This gives 3-formyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methylpiperidino)pyrazolo[1,5-a]pyrimidine in the form of a yellow oil which slowly crystallizes.

$\log P_{(pH = 2.3)} = 4.53$

Example 542



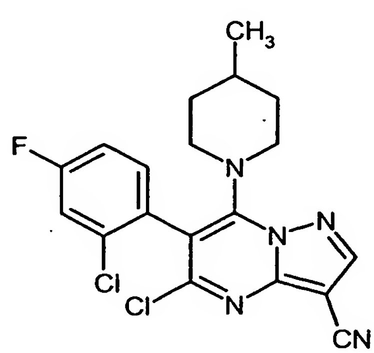
Process (c):

At -50°C and under an atmosphere of argon, 12.2 mmol of diisobutylaluminum hydride (as a 1 molar solution in toluene) are added with stirring to a solution of 11 mmol of 3-cyano-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(3,3-dimethylbut-2-ylamino)pyrazolo[1,5-a]pyrimidine in 150 dichloromethane. After the addition has ended, the mixture is initially stirred at -50°C for another 30 minutes.

At 0°C, saturated aqueous ammonium chloride solution is then added, and the mixture is stirred at 0°C for 2 hours. 1 N hydrochloric acid is then added, and the organic phase is removed. The aqueous phase is extracted three times with dichloromethane. The combined organic phases are washed successively with saturated aqueous sodium bicarbonate solution and with saturated aqueous sodium chloride solution, then dried over sodium sulfate and subsequently concentrated under reduced pressure. The residue that remains is chromatographed on silica gel using methyl tert-butyl ether:petroleum ether = 3:1. This gives 6.4 mmol/58% of theory) of 3-formyl-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(3,3-dimethylbut-2-ylamino)pyrazolo[1,5-a]pyrimidine.

log P = 4.43 / 4.47 (atropisomers)

Example 543

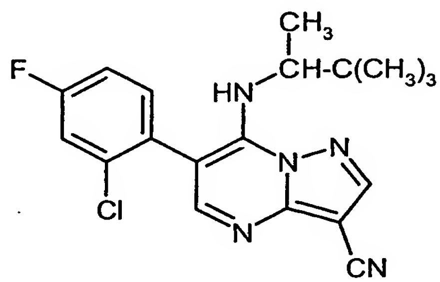


Process (f)

At room temperature, a solution of 5 mmol of 3-cyano-5,7-dichloro-6-(2-chloro-4-fluorophenyl)-pyrazolo[1,5-a]pyrimidine in 10 ml of acetonitrile is added dropwise with stirring to a mixture of 30 ml of acetonitrile, 5 mmol of potassium carbonate and 5 mmol of 4-methylpiperidine. The reaction mixture is stirred at room temperature for 15 hours and then stirred into water. The mixture formed is extracted three times with ethyl acetate. The combined organic phases are dried over sodium sulfate and then concentrated under reduced pressure. This gives 4.28 mmol (86% of theory) of 3-cyano-5-chloro-6-(2-chloro-4-fluorophenyl)-7-(4-methylpiperidino)pyrazolo[1,5-a]pyrimidine.

$\log P_{(pH = 2.3)} = 4.88$

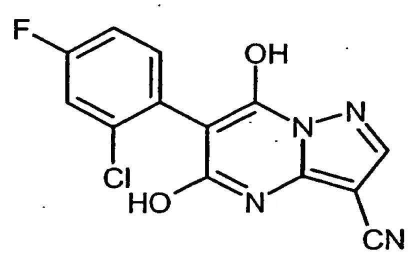
Example 544



The preparation of the compound of the formula given above is carried out by the method given in Example 6.

HPLC: $\log P = 4.78$

Example 545

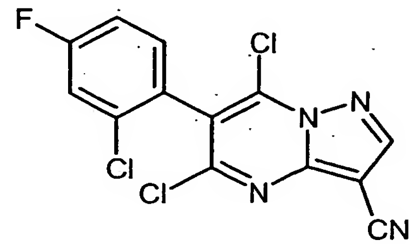


Process (h):

48 g (0.184 mol) of dimethyl 2-chloro-4-fluorophenylmalonate are mixed with 19.91 g (0.184 mol) of 4-cyano-5-aminopyrazole and with 37.55 g (0.203 mol) of tri-n-butylamine, and the mixture is stirred at 180°C for 6 hours. The methanol formed during the reaction is continuously distilled off. The reaction mixture is then cooled to room temperature. At 95°C and 1 mbar, volatile components are distilled off. As a residue, 6-(2-chloro-4-fluorophenyl)-5,7-dihydroxypyrazolo[1,5-

a]pyrimidine-3-carbonitrile is obtained in the form of a crude product which is used without additional purification for further syntheses.

Example 546



Process (g):

The crude 6-(2-chloro-4-fluorophenyl)-5,7-dihydroxypyrazolo[1,5-a]pyrimidine-3-carbonitrile obtained according to Example 8 is dissolved in 367.3 g (2.395 mol) of phosphorus oxychloride. At room temperature, 31.95 g (0.153 mol) of phosphorus pentachloride is added a little at a time. The mixture is then boiled under reflux for 4 hours. The volatile components are distilled off under reduced pressure. Dichloromethane is added to the residue, and the mixture is washed with water. The organic phase is dried over sodium sulfate and concentrated under reduced pressure. The residue is chromatographed on silica gel using 3 parts of cyclohexane and 1 part of ethyl acetate as mobile phase. This gives 21 g of 95.7% pure 3-cyano-5,7-dichloro-6-(2-chloro-4-fluorophenyl)-pyrazolo[1,5-a]pyrimidine.

HPLC: logP = 3.48

^{1}H-NMR (DMSO-d6, tetramethylsilane): δ = 7.44-7.52 (1H); 7.62-7.66 (1H); 7.71-7.77 (1H); 9.03 (1H) ppm.

Use examples

Example A

Venturia - Test (Apple)/protective

Solvents:	24.5 parts by weight of acetone
	24.5 parts by weight of dimethylacetamide
Emulsifier:	1.0 parts by weight of alkylaryl polyglycol ether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amounts of solvents and emulsifier, and the concentrate is diluted with water to the desired concentration.

To test for protective activity, young plants are sprayed with the preparation of active compound at the stated application rate. After the spray coating has dried on, the plants are inoculated with an aqueous conidia suspension of the apple scab pathogen Venturia inaequalis and then remain in an inoculation cabinet at about 20°C and 100% relative atmospheric humidity for 1 day.

The plants are then placed in a greenhouse at about 21°C and a relative atmospheric humidity of about 90%.

Evaluation is carried out 10 days after the inoculation. 0% means an efficiacy which corresponds to that of the control, whereas an efficacy of 100% means that no infection is observed.

In this test, the compounds according to the invention listed in examples 1 and 2 showed, at an application rate of 100 g/ha, an efficacy of more than 90%.

Example B

Botrytis - Test (Bean)/protective

Solvents: 24.5 parts by weight of acetone

24.5 parts by weight of dimethylacetamide

Emulsifier: 1.0 parts by weight of alkylaryl polyglycol ether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amounts of solvents and emulsifier, and the concentrate is diluted with water to the desired concentration.

To test for protective activity, young plants are sprayed with the preparation of active compound at the stated application rate. After the spray coating has dried on, 2 small pieces of agar colonized by Botrytis cinerea are placed onto each leaf. The inoculated plants are placed in a dark chamber at about 20°C and 100% relative atmospheric humidity.

The size of the infected areas on the leaves is evaluated 2 days after the inoculation. 0% means an efficacy which corresponds to that of the control, whereas an efficacy of 100% means that no infection is observed.

In this test, the compounds according to the invention listed in examples 1 and 2 showed, at an application rate of 500 g/ha, an efficacy of more than 90%.

Example C

Podosphaera-Test (Apple)/protective

Solvents:	24.5 parts by weight of acetone
	24.5 parts by weight of dimethylacetamide
Emulsifier:	1 part by weight of alkylaryl polyglycol ether

To produce a suitable preparation of active compound, 1 part by weight of active compound is mixed with the stated amounts of solvents and emulsifier, and the concentrate is diluted with water to the desired concentration.

To test for protective activity, young plants are sprayed with the preparation of active compound at the stated application rate. After the spray coating has dried on, the plants are inoculated with an aqueous spore suspension of the apple mildew pathogen Podosphaera leucotricha. The plants are then placed in a greenhouse at about 23°C and a relative atmospheric humidity of about 70%.

Evaluation is carried out 10 days after the inoculation. 0% means an efficacy which corresponds to that of the control, whereas an efficacy of 100% means that no infection is observed.

In this test, the compounds according to the invention of examples 1 and 2 showed, at an application rate of 100 g/ha, an efficacy of more than 90%.